

THE  
EXTRA PHARMACOPŒIA

---

MARTINDALE  
AND  
WESTCOTT

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VOL. II

SIXTEENTH EDITION

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THE  
EXTRA  
PHARMACOPŒIA  
OF  
Martindale and Westcott.

REVISED

BY

W. Harrison Martindale, Ph.D., F.C.S.

AND

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SIXTEENTH EDITION.

VOL. II

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# INTRODUCTION.

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This volume forms a Supplement to Vol. I. In it are contained matters mostly of the results of Analytical or Experimental investigations.

The subjects dealt with in pages **1** to **137** of this volume are arranged for ease of reference in the same sequence as in the body of Vol. I.

The question of **Poisons** (in the light of the Poisons and Pharmacy Act, 1908) has not received full consideration in this volume, as circumstances hardly necessitate it—though some are indicated. In Vol. I., however, we indicate, as in previous Editions of the Extra Pharmacopœia, into which part of the Poisons Schedule any substance falls, by means of the signs **(P)** and **(P)**.

The **Cross References** in the following pages, *unless otherwise stated*, refer to Vol. II., and in each instance are in heavy type, thus, **100**.

For **List of Abbreviations** see Vol. I. A further list used in the Organic Analysis Chart is given on page **383**.

The subject matter of this volume is indexed in detail in Vol. I., together with the Index of that section of the work.

W. H. MARTINDALE.

W. WYNN WESTCOTT.

London,

January 30, 1915.

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## THERMOMETRIC EQUIVALENTS.

For temperatures below the freezing point of water —

°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.
—	—	—	—	—	—	—	+	—	+
40	40·0	31	23·8	22	7·6	16	3·2	7	19·4
39	38·2	30	22·0	21	5·8	15	5·0	6	21·2
38	36·4	29	20·2	20	4·0	14	6·8	5	23·0
37	34·6	28	18·4	19	2·2	13	8·6	4	24·8
36	32·8	27	16·6	18	0·4	12	10·4	3	26·6
35	31·0	26	14·8	17·778	0·0	11	12·2	2	28·4
34	29·2	25	13·0	—	+	10	14·0	1	30·2
33	27·4	24	11·2	0	0	9	15·8	0	32·0
32	25·6	23	9·4	17	1·4	8	17·8		

For temperature above the freezing point of water :—

°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.
+	+	+	+	+	+	+	+	+	+
1	33·8	39	102·2	77	170·6	115	239·0	153	307·4
2	35·6	40	104·0	78	172·4	116	240·8	154	309·2
3	37·4	41	105·8	79	174·2	117	242·6	155	311·0
4	39·2	42	107·6	80	176·0	118	244·4	156	312·8
5	41·0	43	109·4	81	177·8	119	246·2	157	314·6
6	42·8	44	111·2	82	179·6	120	248·0	158	316·4
7	44·6	45	113·0	83	181·4	121	249·8	159	318·2
8	46·4	46	114·8	84	183·2	122	251·6	160	320·0
9	48·2	47	116·6	85	185·0	123	253·4	161	321·8
10	50·0	48	118·4	86	186·8	124	255·2	162	323·6
11	51·8	49	120·2	87	188·6	125	257·0	163	325·4
12	53·6	50	122·0	88	190·4	126	258·8	164	327·2
13	55·4	51	123·8	89	192·2	127	260·6	165	329·0
14	57·2	52	125·6	90	194·0	128	262·4	166	330·8
15	59·0	53	127·4	91	195·8	129	264·2	167	332·6
16	60·8	54	129·2	92	197·6	130	266·0	168	334·4
17	62·6	55	131·0	93	199·4	131	267·8	169	336·2
18	64·4	56	132·8	94	201·2	132	269·6	170	338·0
19	66·2	57	134·6	95	203·0	133	271·4	171	339·8
20	68·0	58	136·4	96	204·8	134	273·2	172	341·6
21	69·8	59	138·2	97	206·6	135	275·0	173	343·4
22	71·6	60	140·0	98	208·4	136	276·8	174	345·2
23	73·4	61	141·8	99	210·2	137	278·6	175	347·0
24	75·2	62	143·6	100	212·0	138	280·4	176	348·8
25	77·0	63	145·4	101	213·8	139	282·2	177	350·6
26	78·8	64	147·2	102	215·6	140	284·0	178	352·4
27	80·6	65	149·0	103	217·4	141	285·8	179	354·2
28	82·4	66	150·8	104	219·2	142	287·6	180	356·0
29	84·2	67	152·6	105	221·0	143	289·4	181	357·8
30	86·0	68	154·4	106	222·8	144	291·2	182	359·6
31	87·8	69	156·2	107	224·6	145	293·0	183	361·4
32	89·6	70	158·0	108	226·4	146	294·8	184	363·2
33	91·4	71	159·8	109	228·2	147	296·6	185	365·0
34	93·2	72	161·6	110	230·0	148	298·4	186	366·8
35	95·0	73	163·4	111	231·8	149	300·2	187	368·6
36	96·8	74	165·2	112	233·6	150	302·0	188	370·4
37	98·6	75	167·0	113	235·4	151	303·8	189	372·2
38	100·4	76	168·8	114	237·2	152	305·6	190	374·0

Thermometric Equivalents—*continued*.

°C.	°F.	°C.	°F.	°C.	°F.	C.	°F.	°C.	°F.
+	+	+	+	+	+	+	+	+	+
191	375·8	213	415·4	235	455·0	257	494·6	279	534·2
192	377·6	214	417·2	236	456·8	258	496·4	280	536·0
193	379·4	215	419·0	237	458·6	259	498·2	281	537·8
194	381·2	216	420·8	238	460·4	260	500·0	282	539·6
195	383·0	217	422·6	239	462·2	261	501·8	283	541·4
196	384·8	218	424·4	240	464·0	262	503·6	284	543·2
197	386·6	219	426·2	241	465·8	263	505·4	285	545·0
198	388·4	220	428·0	242	467·6	264	507·2	286	546·8
199	390·2	221	429·8	243	469·4	265	509·0	287	548·6
200	392·0	222	431·6	244	471·2	266	510·8	288	550·4
201	393·8	223	433·4	245	473·0	267	512·6	289	552·2
202	395·6	224	435·2	246	474·8	268	514·4	290	554·0
203	397·4	225	437·0	247	476·6	269	516·2	291	555·8
204	399·2	226	438·8	248	478·4	270	518·0	292	557·6
205	401·0	227	440·6	249	480·2	271	519·8	293	559·4
206	402·8	228	442·4	250	482·0	272	521·6	294	561·2
207	404·6	229	444·2	251	483·8	273	523·4	295	563·0
208	406·4	230	446·0	252	485·6	274	525·2	296	564·8
209	408·2	231	447·8	253	487·4	275	527·0	297	566·6
210	410·0	232	449·6	254	489·2	276	528·8	298	568·4
211	411·8	233	451·4	255	491·0	277	530·6	299	570·2
212	413·6	234	453·2	256	492·8	278	532·4	300	572·0

## EQUIVALENTS WITHIN CLINICAL LIMITS.

°C.	°F.	°C.	°F.	°C.	°	°C.	°F.	°C.	°F.
35·0	95·0	36·9	98·42	38·8	101·84	40·7	105·26	42·6	108·68
35·1	95·18	37·0	98·60	38·9	102·02	40·8	105·44	42·7	108·86
35·2	95·36	37·1	98·78	39·0	102·20	40·9	105·62	42·8	109·04
35·3	95·54	37·2	98·96	39·1	102·38	41·0	105·80	42·9	109·22
35·4	95·72	37·3	99·14	39·2	102·56	41·1	105·98	43·0	109·40
35·5	95·90	37·4	99·32	39·3	102·74	41·2	106·16	43·1	109·58
35·6	96·08	37·5	99·50	39·4	102·92	41·3	106·34	43·2	109·76
35·7	96·26	37·6	99·68	39·5	103·10	41·4	106·52	43·3	109·94
35·8	96·44	37·7	99·86	39·6	103·28	41·5	106·70	43·4	110·12
35·9	96·62	37·8	100·04	39·7	103·46	41·6	106·88	43·5	110·30
36·0	96·80	37·9	100·22	39·8	103·64	41·7	107·06	43·6	110·48
36·1	96·98	38·0	100·40	39·9	103·82	41·8	107·24	43·7	110·66
36·2	97·16	38·1	100·58	40·0	104·0	41·9	107·42	43·8	110·84
36·3	97·34	38·2	100·76	40·1	104·18	42·0	107·60	43·9	111·02
36·4	97·52	38·3	100·94	40·2	104·36	42·1	107·78	44·0	111·20
36·5	97·70	38·4	101·12	40·3	104·54	42·2	107·96		
36·6	97·88	38·5	101·30	40·4	104·72	42·3	108·14		
36·7	98·06	38·6	101·48	40·5	104·90	42·4	108·32		
36·8	98·24	38·7	101·66	40·6	105·08	42·5	108·50		

The Reaumur scale (with zero at freezing point of water and the boiling point of water being 80°) is now little used.

To convert a temperature in Centigrade into Fahrenheit multiply by  $\frac{9}{5}$  and add 32.

Conversely to transpose Fahrenheit into Centigrade subtract 32 and multiply by  $\frac{5}{9}$ .

To convert Centigrade into Reaumur multiply by  $\frac{4}{5}$ .

To convert Reaumur into Centigrade multiply by  $\frac{5}{4}$ .

To convert Fahrenheit into Reaumur subtract 32 and multiply by  $\frac{4}{9}$ .

To convert Reaumur into Fahrenheit multiply by  $\frac{9}{4}$  and add 32.



# ANALYTICAL ADDENDA TO MATERIA MEDICA CONTAINED IN VOL. I.

## ACETANILIDUM.

**Acetanilide and Methylene Blue Tubes.** *Syn.* TUBES TÉMOINS.

Sealed glass tubes filled with Acetanilide Powder and containing in addition in the centre a small pinch of Blue Dye. These are used to place in sterilisers to determine whether sterilisation has been adequate and has penetrated into the centre of the dressings. Acetanilide melts at  $113^{\circ}\text{C}.$ , hence if this temperature has been reached the contents of the tube on removal should be evenly blue throughout.—*c.f.* B.M.J. i./11,879.

**Tests for Recognition.**—See Organic Analysis Chart and Corroborative Tests.

## ACIDUM BENZOICUM.

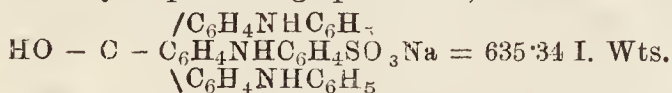
**Tests.**—Should not develop odour of benzaldehyde when warmed with its own weight of potassium permanganate and ten times its weight of dilute sulphuric acid (*Off.* test for cinnamic acid). Solution in sulphuric acid when gently warmed should not turn darker than light brown, U.S. Commences to sublime at  $100^{\circ}\text{C}.$  (U.S.) and melts at  $120\text{--}122^{\circ}\text{C}.$

**USE AS PRESERVATIVE.**—Wiley in America was in favour of its use.—L. i./09,508. Lehmann, *Chem. Zeit.*, 1908, and Vietinghoff-Scheel, *ibid.*, 1909, showed that the Acid and Sodium Benzoate are not harmful. 0.1% is sufficient to preserve meat and butter. 0.05% is sufficient for fruit and fruit syrups. May be injurious if given over a lengthy period.—L. i./09,572. See also P.J. ii./08,252.

**Detection of, in Foodstuffs.**—Extract with a mixture of ether and petroleum ether in equal parts; this evaporated may contain saccharin (taste), salicylic acid (by its colour with ferric chloride), and benzoic acid—recognised by odour, crystalline form, and conversion into anilin blue by heating with Rosanilin and Anilin. This is Triphenyl-Rosanilin,  $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O} = 547.294$  I. Wts. or  $\text{C}_{20}\text{H}_{16}(\text{C}_6\text{H}_5)_3\text{N}_3(?) = 529.278$  I. Wts. Its Hydrochloride is called Opal Blue, *Syn.*, Spirit Blue, being soluble in spirit.

**Water-Soluble-Blue** is obtained by converting Spirit Blue (above mentioned) into Triphenyl-Rosanilin-Trisulphonic Acid by treatment with Sulphuric Acid, and is usually supplied as the Ammonium Salt. (Simpson.)

**Nicholson's Blue** is the Sodium Salt of Triphenyl-Rosanilin-Monosulphonic Acid made by sulphonating Spirit Blue, almost in the cold, composition:



Nicholson's Blue is dyed on wool or silk from a slightly alkaline or neutral bath. The goods are washed and then developed in a bath acidulated with Sulphuric Acid. The ordinary water-soluble blues dye from an acid bath.

Dried Cranberries contain as much as 0.45% Benzoic Acid.—L. i./09,1701.

**Siam Benzoin.**—Of the four varieties in commerce the botanical source of only one up to the present has been accurately ascertained. Owing to difficulty of penetrating into the centre of Siam botanical specimens of trees cannot be obtained. The fruit of the tree yielding Siam Benzoin is totally different in character from that of *Styrax Benzoin*. Hitherto it was thought that the tree yielding Siam Benzoin was identical with that yielding the Sumatra product.

The only source of Siam Benzoin of commerce is *Styrax Tonkinense*, Craib, found in the district between Luang Prabang and Hanoi. *S. Benzoides* of N. W. Siam yields a fragrant resin, but it is not certain that it enters commerce. The method of preparation with hog's marrow would account for the characteristic appearance of Siam Benzoin.—E. M. Holmes, P.J. ii./13, 802,804.

## ACIDUM BORICUM.

**Boron** has an abnormal value in its temperature co-efficient of resistance. A small piece of fused Boron mounted in series with an electric lamp obstructs nearly all the current, but on warming the Boron the resistance is reduced and the lamp lights. A filament of Boron at ordinary temperatures will show a resistance of 5,620,000 ohms, but when warmed to a dull red heat the resistance drops to 5 ohms. A splinter of Boron is almost as hard as a diamond. It will easily scratch the very hard substance Carborundum.—L. ii./12, 1822.

Scientific data on the various Boric Acids.—A. Holt Manch., Phil. Soc., Feb. 21/11, per Na. Mar. '11, 66.

Lead as impurity is of importance. Usual limit is 10 parts per million.

C. A. Hill, C.D. ii./14, 17, considers 20 parts per million sufficiently stringent.

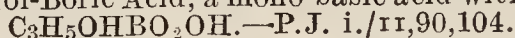
Tankard goes fully into the subject of Boric and other preservatives in milk, butter, potted meats and the like. It is stated that in Hull fully  $\frac{2}{3}$  of the butter sold is entirely free from preservatives. A curious instance of a preservative containing Potassium Metabisulphite 30%, Anhydrous Sodium Sulphate 60%, Powdered Glass 2 to 7 $\frac{1}{2}$ % is given,—due to impurity in using "glass gall" for Sodium Sulphate.—P.J. ii./11, 5. ("Glass gall" is the neutral salt skimmed off surface of molten crown glass.)

**Detection of Boric Acid.** See also **Milk Analysis**, pp. 270, 271.

Detection of minute traces of Boric Acid by Tincture of Mimosa Flowers made by warm maceration (10 minutes on water bath) of 5 Gm. first in 50 Cc., and then with 40 Cc. Alcohol 95% after decanting.—For details *vide* P.J. i./14, 31.

### Glycerinum Acidi Borici.

The reaction between Boric Acid and Glycerin leads, it is thought, to the formation of Glycerol-Boric Acid, a mono-basic acid with formula



### Sodii Biboras. Borax.

Forty samples contained Arsenic from 0 to 160 parts per million. A fair standard limit should be 4 parts per million.—Southall's Lab. Report 1912.

*For further information on Boric Acid and its preparations, see Vol. I.*

## ACIDUM CARBOLICUM.

**Quantitative Estimation of Phenol.**—This may be effected by converting it into Tribromphenol  $\text{C}_6\text{H}_2\text{Br}_3\text{OH}$ :—

Dissolve Phenol 1.567 Gm. in water sufficient to make 1000 Cc. Place 25 Cc. of the Solution in a 200 Cc. stoppered bottle, add 30 Cc. of N/10 Bromine Solution (**Koppeschaar's Solution**) and shake repeatedly for half an hour; then add 5 Cc. of 20% Potassium Iodide Solution, shake well, add 1 Cc. Chloroform and titrate excess of Iodine with N/10 Thiosulphate. Subtract the number of Cc. required from thirty; the remainder equals the number of Cc. N/10 Bromine used up. This multiplied by 4 gives the percentage of absolute Phenol (*i.e.*, 1 Cc. N/10 Br. = 0.001567 Gm. Phenol).

The process works satisfactorily,—we obtained, with a sample of detached crystals (M.Pt. 41° C.), 98% as an average of three determinations.

**Koppeschaar's Bromine Solution** is made as follows:—

Dissolve Potassium Bromate 3.2 Gm. and Potassium Bromide 50 Gm. in Water 900 Cc. To standardise place 20 Cc. in a 250 Cc. bottle with Water 75 Cc. and 5 Cc. Pure Hydrochloric Acid. Shake a few times, quickly introduce 5 Cc. of 20% Potassium Iodide Solution and titrate the Iodine set free by N/10 Sodium Thiosulphate. Dilute the Bromine Solution so that equal volumes of it and the N/10 Thiosulphate exactly correspond in the conditions of the test.—*c.f.*, U.S.P., 1905, p. 547.

Excretion of Phenol after poisoning by.—Dublin Jl. Med. Sci., May, 1914. L. i./14, 1585.

## ACIDUM HYDROCYANICUM.

**Volumetric Estimation.**—Titrate about 1 Gm. (accurately weighed, kept slightly alkaline with Sodium Hydroxide throughout the test), with N/10 Silver Nitrate Solution, until a permanent Silver Cyanide precipitate is formed.



The soluble double Salt,  $\text{AgCN} \cdot \text{NaCN}$ , is intermediate.  $\text{AgNO}_3 = 2\text{HCN}$  or 1 Cc. N/10  $\text{AgNO}_3 = 0.00537$  Gm.  $\text{HCN}$ .

Borax Solution in excess is added to Hydrocyanic Acid before titration with Silver Nitrate. Suitable for Cherry Laurel Water.—P.J. ii./05,910.

**Quantitative Estimation of Hydrocyanic Acid in the blood and tissues of animals post mortem.** The method is colorimetric and depends on reaction between Potassium Cyanide and Picric Acid. (Liebig's *Annalen*, CX. p. 289 (1859). A Color Scale for comparison is made by mixing equal volumes of recently titrated 1/1000  $\text{HCN}$ . and Picrate mixture (equal volumes of 0.5% Picric Acid and 5% Sodium Carbonate). This stock solution (T 500) is further diluted (T 1, 2, etc.). The estimation is made by matching the color of the given fluid or of its distillate into Picrate Mixture with that of the color scale.—A.D. Waller, *Phys. Proceedings*, June 18, 1910

**Detection of Traces of Hydrocyanic Acid.**

A comparison has been made of the delicacy of the Prussian blue as compared with the picrate test for hydrogen cyanide, from which it appears that the former is of at least equal delicacy to the latter.

By evaporating the Alkaline Cyanide Solution to almost complete dryness, adding 2 per cent. Ferrous Sulphate, leaving *in the cold* for ten minutes and acidification, evidence of the presence of 0.000002 gm. of  $\text{HCN}$  may be obtained. The Ferro-Cyanide reaction may be used for the detection of Hydrogen Cyanide in the blood and brain of poisoned animals with equal efficiency to the Picrate method as applied to the same purpose by Waller.—G. D. Lander and A. E. Walden. *Chem. News*, May 19/11, p. 240.

**Delicate Test for Hydrocyanic Acid.**—A few drops of phenolphthalein solution made alkaline with Sodium Hydroxide added to liquid to be tested. If red colour be produced on adding Cupric Sulphate Solution 1 in 2,000 (due to oxidation into phenolphthalein) Hydrocyanic Acid is proved to be present.

Phenolphthalein is made by reducing phenolphthalein with Zinc in alkaline solution.—P.J. i./05,721.

**Method of Horticultural Use.**—Employing Sodium Cyanide and acid.—P.J. ii./08,722.

Hydrocyanic Acid is used for fumigating ships containing grain, foodstuffs, etc.,—it is the best vermicide for the purpose, destroying rats, fleas, etc. It has no ill effects on dry grain, but moist food, *e.g.*, butter, milk, etc., is liable to absorb the gas. It has been used in South Africa to destroy vermin in railway carriages.—P.J. ii./12,804.

## ACIDUM LACTICUM.

P. G. V. requires (with Sp. Gr. 1.21 to 1.22), about 75 per cent. of Lactic Acid and 15 per cent. of *Lactic Anhydride*, calculated as Lactic Acid. Assay-process: 5 Gm. of Lactic Acid is diluted with water to 50 c.c.; 20 c.c. of this mixture is neutralised with N/1  $\text{KOH}$ , using at least 16.6 c.c. of test-solution (= 74.7% of Lactic Acid). The neutral liquid is warmed for one hour on the water-bath, after adding 10 c.c. N/1  $\text{KOH}$ . For neutralisation, 6.7 c.c. of N/1  $\text{HCl}$  should be required = 15% Lactic Anhydride, calculated as Lactic Acid, 0.09005 Gm. of which corresponds to 1 c.c. N/1  $\text{KOH}$  (using phenolphthalein as indicator).

Lead should not exceed 10 parts per million.

Assay of Lactic acid.—Am. Jl. Ph., Jan., 1911, 14.

For further information re Lactic Acid vide Vol. I.

## ACIDI LACTICI BACILLI.

**Lactic Acid Bacilli Preparations.**

Prof. Elie Metchnikoff, in his work "The Prolongation of Life," evolved a theory of arresting the growth of putrefactive (alkaline) organisms in the intestines, and hence stimulating intestinal digestion and diminishing toxic absorption from the bowel by acclimatising the (harmless) Lactic Acid Bacillus. He takes as his starting-point that the newly-born infant has sterile intestines and on partaking of the first drop of mother's or cow's milk these commence to be infected. He then discusses the evils resulting from putrefied food, some of the recipients dying from the effects; others if their resistance be

sufficient, saving their lives after experiencing a severe attack of cholera. The word 'acid' makes its appearance—*i.e.*, in connection with the custom prevailing from early times of preserving food with vinegar—the product of bacteria to 'ward off putrefaction.' It is further pointed out that substances themselves producing a preservative acid—*e.g.*, milk,—can be made into others—*e.g.*, cheese—which can be kept for longer or shorter periods of time. 'Kwass,' of which black bread is the main ingredient, is the chief beverage in Russia in the summer. It contains Lactic Acid. Other instances are given with the conclusion, Why not arrest putrefaction in the digestive tract as with the conserve?

Experimental consumption of large quantities of Lactic Bacilli showed that intestinal putrefaction was diminished.

It was found that with a normal diet the *Bacillus* appeared in the stools in three to four days after it had been begun to be consumed regularly with the food; that it took eight days to become properly acclimatised in the intestine, and that when this had taken place it would continue to live and thrive for twelve more days without another dose being swallowed, afterwards gradually disappearing. Regular administration caused increase in weight and bulk of fæces.

Lactic Acid, as such, has been employed for years past in dyspepsia, enteritis, &c., as also in diabetes, and locally in tuberculous ulceration of the larynx.

The conclusion was that as organisms of putrefaction only increase with difficulty in neutral or acid media, the most feasible procedure would be to introduce a Lactic Acid organism (growing in a sugar medium) into the human organism to arrest the proliferation of harmful bacteria. The bacillus known as the **Bulgarian Bacillus** (*B. Caucasicum*), isolated by Cohendy and independently by Massol from 'Yoghourth,' a form of soured milk, was deemed most suitable, as it is the best acid producer. The acid it produces is the optically inactive variety. It is a hardy organism resisting the stomach juices and its own acidity to a marked degree.

According to Hewlett it occurs apparently in various forms. In natural soured milks for example:—

- (1) *B. Bulgaricus* and *B. Massol* from Bulgarian Yohgurt and Maya.
- (2) *Streptobacillus lebenis* from Egyptian leben.
- (3) *Bacillus Mazun* from Armenian mazun.
- (4) The "Granule" bacillus from Bulgarian Yoghurt.
- (5) *Bacterium Sirdons* from Sardinian Gioddu (grixoni).
- (6) *Bacterium Lactis Acidi* (Leishman).

are probably varieties of only one species.—*B.M.J.* ii./10, 1584; *L.* ii./10, 402.

**Buttermilk** in many countries, **Kephir** or **Koumiss**, *vide Vol. I. p. 544*, the Egyptian 'Leben Raib,' 'Prostokwocha,' and 'Varenetz,' of Russia, **Yoghourth** (Yohourth) of the Balkans, and many others were forerunners of the curdled milk treatment, which recently attracted so much attention. It is believed that the Bulgarian peasant consumes as much as 10 Gm. of Lactic Acid daily in his diet of Yohourth.

**Kephir Fungus** or grains occurs in small yellow nodules. A recent bacteriological examination showed the presence of Lactic Acid Bacilli with a few yeast organisms and practically no cocci.

These sour milks, as a rule, contain yeasts in small proportions, and *ergo* alcohol—the same remark applies to the artificially soured milks.

Emerson advises the presence of a carefully selected strain of yeast as a useful therapeutic aid in many affections.

The **Bulgarian Bacillus**, according to Metchnikoff, will produce as much as 2.5 Gm. of Lactic Acid per 100 Cc. of milk.

Succinic, acetic and formic acids are also formed by it in small quantity. This bacillus has no action on albuminoids (casein, &c.) nor fats, nor does it produce alcohol or acetone. It does not attack saccharose (cane sugar) or maltose; it is therefore useless to add cane sugar in the hope of increasing Lactic Acid yield. For flavouring purposes the *B. paralactic* (*B. Güntheri*) is used in conjunction.

**Günther's Bacillus** is found in abundance in all spontaneously coagulated milk and is an important Lactic Acid producer.

It modifies the condition of the curd formed, and hence is a useful addition, but it appears to die out in the finished product. It produces pure dextrorotatory Lactic Acid (no other acid) from grape and milk sugar.



Hüppe's Bacillus is another Lactic Acid organism.

It is almost always present in milk which has soured spontaneously. This organism, sometimes called specifically the *B. Acidi Lactici*, differs from *B. Güntheri*, by its comparative ease of cultivation upon ordinary nutrient media.

Léon Massol took cultures of the Bulgarian Bacillus to Paris, and these gave Metchnikoff the starting point for his researches on the efficacy of soured milk.—B.M.J. i./10,57.

The characters of the chief Lactic Acid organisms may be tabulated:—

ORGANISM AND SYNONYMS.	APPEARANCE.	PROPERTIES.
<i>Bacterium Caucasicum</i> (Kern); <i>syn.</i> Massol's Bacillus, <i>syn.</i> Bouchard's Bacillus, <i>syn.</i> Bulgarian Bacillus.	Large square-shaped, 5 to 6 $\mu \times 1 \mu$ showing vacuoli, slightly motile. +Gram staining.	Appears to take a little time to establish itself, but ultimately is the omnipresent bacterium in milk. It is a strong lactic acid producer.
Hüppe's Bacillus: <i>syn.</i> <i>B. Acidi Lactici</i> . <i>Streptococcus Leberis</i> may be closely allied.	Coccoid shape 0.4 to 0.6 $\mu \times 0.6$ to 2 $\mu$ . Usually in pairs, rarely longer chains, non-motile. +Gram staining.*	Causes bitterness, breaks up fat and proteolytic substances.
<i>Bacterium Güntheri</i> ; <i>syn.</i> <i>B. Acidi Puralactici</i> (Kozai).	Short rods, 1 $\mu \times 0.5$ to 0.6 $\mu$ , with pointed ends, in pairs or short chains non-motile. -Gram staining.	Gives a smooth, non-leathery form of curd. It appears to be killed off to some extent in the curdling of milk, being probably ousted by <i>B. Caucasicum</i> .

### Methods of Examination of Lactic Acid Bacilli Preparations.

#### 1.—ORGANISMS PRODUCED AND CURD FORMATION.

Loopfuls of the milk, treated with a crushed Lactic Acid Bacillus tablet (*vide* Vol. I.), are to be examined after ten and twenty-four hours' cultivation.

The best Staining Method to employ is that of Gram *q.v.*, using 1% neutral red as counterstain. The Gram-staining organisms take on a deep violet, and the rest of the field is a reddish pink, less diffuse than that with eosin, which is often used as a counterstain. A copious growth of *B. Caucasicum* is essential, with exclusion of other bacteria. Curd formation should also be satisfactory.

The property of producing lactic acid is common to a vast number of organisms (*cf.* L. ii./08,957).

#### 2.—ESTIMATION OF LACTIC ACID.

The Pasteur Institute found in soured milk, made according to Metchnikoff, 1% of lactic acid when ready for consumption. More is formed if longer time allowed (*vide antea*).

The amount obviously depends on the content of lactose, the average of this constituent being 4 per cent. The decomposition of lactose in milk into lactic acid is a complex matter. In any case nature will not allow an optimum yield, as the bacilli kill themselves by the acid they produce—the maximum acid formation being reached in about thirty-six hours.

*It is, however, not so much a question of the quantity of acid produced as the assurance that the culture used is active and capable of*

\*The Hüppe's Bacillus with which we have worked has been found to stain well by Gram's method, but opinions differ.

thoroughly establishing itself in the intestines to the exclusion of harmful bacteria, as evidenced by bacteriological examinations of the excreta.

Wynter Blyth says the maximum amount of lactic acid formed in ordinary conditions (from milk) appears to be 0·8 per cent., which agrees with our own finding.

Milk, it should be noted, is amphoteric in reaction on account of its content of alkali phosphate. Phenolphthalein can be used as an indicator in titrating, but the end reaction is a little difficult to determine—it requires to be carefully looked for : 20 Cc. of the milk is a convenient quantity to titrate, using  $\frac{N}{10}$  Soda.

### 3.—CASEIN RENDERED SOLUBLE.

At the Pasteur Institute 38 per cent. of the casein in milk could be rendered soluble by treatment with lactic-acid organisms (Metchnikoff, p. 180) Herschell states that as much as 50 per cent. of it is converted into albumose and peptone by this means.

For further details *vide* a paper by the author, 'Lactic Acid Organisms.'

### 4.—PHOSPHATE RENDERED SOLUBLE.

Metchnikoff states that 68% of the calcium phosphate (which he terms the chief mineral substance of milk) was rendered soluble during fermentation by his process.

Our investigations gave results closely approximating this statement.

It appears that in the district around Milan spontaneously curdled milks are not used to any extent nor milks prepared by special ferments. In Sardinia, however, the people prepare and make a continuous diet of (for lack of anything better) Gioddu Mezzoraddu, or Micariatu, which are the products of fermentation due to *Saccharomyces Sardons* and to *Bacillus Sardons* and *Mazun*, and which resemble in composition the Lebenraib of Egypt, the Prostokwacha and Varenetz of the Russians, the Kephir of the Caucasians, the Koumiss of the Tartars, and the Mazun of the Armenians. At Milan the grape ferment is in demand, at Turin Blastoinvertin (*Saccharomyces invertens*) in Lombardy Kephir, and at Piedmont the true Yoghourt.

From Greece we learn that Yoghourth is much in use both as a food and for therapeutic treatment. It is prepared there by adding a little lemon-juice to fresh milk, which is then kept warm for eight hours, forming a curd which is the first stage in the manufacture. From the curd thus formed a tablespoonful is mixed with boiled milk, and this procedure is repeated several times, with fresh milk on each occasion, until a Yoghourth of suitable consistence is obtained. Small spoonfuls of this latter product are added to wooden or earthenware pans containing milk which has been boiled and is still slightly warm. This forms the commercial Yoghourth, which curdles in four hours at 35° C. It has at first a sweetish taste, becoming extremely acid after twelve hours. In order to keep it, which one may do for as long as from five to eight days, it is poured into little bags of cotton from which the whey filters, the product thereby becoming thicker and of better-keeping qualities. Yoghourth prepared from sheep's milk is highly esteemed as a milk-food by the Greeks.

## ACIDUM PHOSPHORICUM.

*Volumetric titration* with normal Potash Solution using Phenolphthalein as indicator is well known to give very variable results especially when considerably diluted or in presence of ionisable salts. An iodometric estimation based on reaction which takes place between Phosphoric Acid, Potassium Iodide and Potassium Bromate, especially if allowed to proceed at 20° C. for 2½ to 3 hours, is more reliable.

5 Cc. of the Acid in 5% dilution in a 150 Cc. stoppered bottle with 2 Gm. (approx.) of Potassium Iodide, 5 Cc. of Saturated Potassium Bromate Solution and 30 Cc. of water, left securely stoppered for 2½–3 hours and Iodine liberated titrated with Sodium Thiosulphate Solution —  $6\text{H}_3\text{PO}_4 + 6\text{KI} + \text{KBrO}_3 = 6\text{KH}_2\text{PO}_4 + 3\text{I}_2 + \text{KBr} + 3\text{H}_2\text{O}$ . 98·064 of Acid = 126·92 parts l. = 248·22  $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$ , or 1 Cc.  $\frac{N}{10}$   $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$  (0·024822 Gm.) = 0·0098064 Gm.  $\text{H}_3\text{PO}_4$ .—Am. Jl. Ph., April '08, p. 151. (Figures revised by us to 1915 International Wts.).



*Off.*—A process is now given for titrating with N/1 Sodium Hydrate in presence of Sodium Chloride.

#### Detection of Arsenic Acid in presence of Phosphoric Acid.

The solution of the alkali salts of the two acids, rendered faintly acid with Acetic Acid, is reduced to small volume, and treated with 10–15 Cc. of a concentrated solution of Ammonium Nitrate. Raise to boiling and add about 1 Gm of Ammonium Molybdate. When this has dissolved, the liquid is boiled for about 1½ minutes. If Arsenic Acid is present, a white precipitate forms. By this method 0·002 Gm. of Arsenic Acid can be detected in the presence of a large quantity of Phosphoric Acid. Salts of Ca, Sr and Mg. do not invalidate the test, but render it rather less delicate.—J.C.S.A. ii /10,896.

**Metaphosphoric Acid**  $\text{HPO}_3$  = 80·048 I. Wts. is equivalent to *Glacial Phosphoric Acid*, and is employed as an Albumin Test. (*vide* p. 210).

**Pyrophosphoric acid** is formed as an intermediate compound in the hydration of metaphosphoric acid. The hydration does not take place according to any simple scheme, and a method of estimating meta acid in a solution of all three varieties by means of barium chloride is described. From the depression of the freezing point of aqueous solutions of various varieties of pyro and meta acids, it appears that, when these acids are prepared by dehydration of orthophosphoric acid there occurs association of the molecules, but when prepared by decomposition of the lead salts by hydrogen sulphide simple molecules result.—Myers & Hold, Manch. Phil. Soc. per Na. March, 11, 66.

### ACIDUM SALICYLICUM.

**Use as Preservative.**—Its use as food preservative has the disadvantage of sometimes giving the odour of phenol. **Detection of.**—Concentrate liquid (distil off any alcohol) in presence of Alkali and Sodium Chloride, acidify and shake out with Chloroform, evaporate and add Ferric Chloride Solution, red colour.—P.J. ii./05,279. Its use to preserve foods, where otherwise rapid decomposition would occur in hot weather, is upheld by some—personally we do not favour its employment. *See also Organic Analysis Chart.*

A Departmental Committee inquired into use of preservatives and colouring matters added to foods. Not more than one grain per pint of liquid and 1 grain per pound of solid food is permissible. The presence of Salicylic Acid may impair digestion, but is said not to be injurious. For references *vide* Edn. XV., Vol. II., p. 12. *Cf. Acidum Benzoicum.*

Methods of detecting Artificial from Natural Salicylic preparations.—Am. Jl. Ph. Sept. 1908. P.J. ii./08,585.

**Antiseptic Power** *see* Chapter on.

### ACIDUM ACETYL-SALICYLICUM.

**Test for Acetyl-Salicylic Acid and its Salts.**

A solution yields a buff-coloured precipitate with Ferric Chloride until hydrolysed by the addition of a little Hydrochloric Acid, which yields the typical violet colour of Salicylate (developing particularly on warming)

Ferric Aceto-Salicylate is hence less soluble than the Salicylate.

The Ferric Chloride Test for **free Salicylic Acid in Acetyl-Salicylic Acid**, e.g., as in the P.G.V., is inefficient to prevent adulteration, etc., in that the addition of Borax, Sodium Phosphate, Tartaric Acid, Citric Acid and other Oxy-acids will readily prevent or mask the colour ordinarily produced with Ferric Chloride.—Pharm. Ztg., 1912, v. 57, p. 311.

#### Liberation of Salicylic Acid from Acetyl-Salicylic Acid and its salts in dilute Acid and in Water.

Whilst engaged in writing the last Edition we conducted a large amount of experimental work on this subject in 1911.

Acetyl-Salicylic Acid is commonly stated to be therapeutically

active only when reaching the intestines which it is said to do unchanged—this statement being doubtless based on the assumption that it is more readily decomposed by alkalis. In 1903 experiments indicated that there is distinct decomposition in presence of the acidity of the stomach. It was found that agitated with water at 17° C., it is not decomposed into Salicylic and Acetic Acids immediately, but that the hydrolytic action of the water can be recognised after an hour's contact. Trituration before treatment with water appears to facilitate the decomposition. At 37° C. the hydrolysis is more evident, while with artificial gastric juice—(Pepsin 1, Hydrochloric Acid 10, Water 500) hydrolysis is still more rapid, the acid becoming at least partially decomposed.

Our own work tended in the same direction as the above data. The Pepsin was eliminated from our experiments as it does not affect the matter.

Our observations were as follows:—

Hydrolysis of Acetosalicilic Acid takes place slowly both in the presence of plain water and in 0.2% HCl. The amount of decomposition in each case was obtained by colorimetric estimation with Ferric Chloride, using 1 in 50 solutions of Salicylic Acid and Acetosalicilic Acid.

After 1 hour at 37° C.	0.8%	of Acetosalicilic Acid hydrolysed in	Water.
„ 1 „ „	5.0%	„ „	„ 0.2% HCl.
„ 2 hours „	2.0%	„ „	„ Water.
„ „ „	5.0%	„ „	„ 0.2% HCl.
„ 3½ „ „	2.6%	„ „	„ Water.
„ „ „	5.0%	„ „	„ 0.2% HCl.
„ 4½ „ „	2.8%	„ „	„ Water.
„ „ „	5.0%	„ „	„ 0.2% HCl.

By boiling the Acid from the 4½-hours test for about 1 minute it gave 7.5% hydrolysed.

After 22 hours 13% hydrolysed in Water.

„ „ „ 33% „ „ 0.2% HCl.

And so on, gradually increasing.

To ensure that the Ferric Chloride colouration should not be interfered with by presence of the Hydrochloric Acid, the comparisons were made with a 0.2% HCl solution of Salicylic Acid, in the case of the HCl. solutions of Acetosalicilic Acid. A further addition of 0.4% HCl. was required to decolourise the solutions. It was found that at least 2½% HCl. must be present to discharge or prevent the colour completely working with a 1 in 1000 solution of Salicylic Acid only. This is probably due to mass action. Taking the case of 5% hydrolysis, the amount of Salicylic Acid would only be 1 in 10,000 and one would expect that less HCl. would be required to discharge the iron colour than when the Salicylic Acid is increased ten times as in a 1 in 1000 solution.

Whilst these experiments were proceeding, G. Chambers, working independently at Toronto, came to very similar conclusions to our own, *vide* B.M.J. i./12,121. He maintains that the substance is absorbed as such without decomposing. Given in solution (which is not very practicable in view of the slight solubility) he claims it passes rapidly into the intestine (pharmacological action being seen in half an hour) and is absorbed there for the most part unchanged. We hold that on reaching the intestine there must be a splitting up of the acid and the formation of Sodium Salicylate, however slight, at this stage, either from the nascent Salicylic Acid previously



formed in passing through the stomach or by the splitting up of the Acetylated Acid by action of the alkali.

The **general conclusion** of our investigation is clear—namely, that in taking a dose of Acetyl Salicylic Acid *the amount split up whilst passing through the stomach does not exceed 5% of the amount taken*. The Salicylic Acid thus formed and the rest of the acetylated substance passing on unchanged—the latter after hydrolysis in presence of the alkali—are in all probability absorbed into the tissues as Sodium Salicylate.

**CALCII ACETO - SALICYLAS.** *Syn.* \*TYLCALSIN and  
**LITHII ACETO-SALICYLAS.** *Syn.* \*TYLLITHIN.

Hydrolysis :—

Working on lines identical with those used in the case of Acetosalicyllic Acid *q.v.* in a lengthy investigation of the subject of the probable splitting up which occurs *in vivo*—the following amounts of hydrolysis were obtained:—  
 After 4½ hours at 37°C. After 22 hours

Acetosalicyllic Acid in 0.2% HCl	5.0% hydrolysed ;	33%
in Water	2.8% ;	13%
Tylcalsin in 0.2% HCl	1.8% ;	22.5%
in Water	4.4% ;	41.2%
Tyllithin in 0.2% HCl	2.6% ;	28%
in Water	5.3% ;	56%

It is interesting to note that the amounts hydrolysed in the 4½ hours are slight in all cases and show no great difference. Hence the alkaline salts may be quite as useful in physiological action as the acid itself, and by reason of their greater solubility—in particular the calcium salt—should possess distinct advantage for prompt action.

At commencement of the test, *i.e.*, immediately on dissolving———

Acid Aceto-salicyllic showed *no* hydrolysis.

Tylcalsin                   "                   0.6%                   "

Tyllithin                   "                   1.6%                   "

(The presence of Hydrochloric Acid does not interfere with the delicacy of the Ferric Chloride Test in the 22 hour results where the greater hydrolysis is seen. For colorimetry extremely dilute solutions are necessary,—the mixture had to be diluted 50 times, hence the Hydrochloric Acid only amounts to 0.004% and as already stated it requires 0.6% to prevent the colour. In any case the 22 hour results were only determined for corroboration,—we are concerned with the time the medicine would take to exert its physiological action—*i.e.*, in certainly less than 4½ hours.

For further details on Aceto-Salicyllic Acid and its Salts see Vol. I.

## ACIDUM SULPHURICUM.

This Acid is used commercially for the production of glucose which enters into the manufacture of beer. Owing to it being made from Pyrites, it contaminated the glucose and thence the beer with arsenic in 1900.

Report of Royal Commission on arsenical poisoning see B.M.J. ii./03,1557, 1610 ; L. ii./03,1674, *vide* also Arsenium, p. 24.

**Sulphur Dioxide and Trioxide** in the products of combustion of coal gas are detrimental to health and to metal fittings, furniture, etc. Prior to 1906 Parliamentary restriction prevented the presence of more than 20 grains per 100 cubic feet. This restriction was removed with result that the content of Sulphur went up. The resulting gas was so detrimental that for their reputation the Gas Companies started partial purification again. Even now the content is 24½ grains per 100 cubic feet. The Sulphur in the gas is present as Carbon Bisulphide. The South Metropolitan Gas Company intend to supply the whole of their gas free from Sulphur compounds.—L. i./13,1270, 1503.

Sulphurous Acid in Coal Gas Products.—Estimation amounted to 0.002 mgr. per cubic metre of the gas—in addition to Sulphuric Acid.—P.J. ii./12,711.

Sulphuric Acid Manufacture, Theory of, Reynolds and Taylor.—P.J. i./12, 486.

Volatility of Sulphuric Acid when used in vacuum desiccator has been found to be quite perceptible.—P.J. ii./13,497.

### **Sulphuric Acid, Solidified.**

Sulphuric Acid mixed with 25% to 30% Kieselguhr becomes completely solid—suitable for transport.—P.J. i./13,206.

Sulphuric, Nitric and Nitrous Acids in admixture, Determination of.—P.J. i./13,469.

Sulphuric Acid, Fuming,  $\text{H}_2\text{S}_2\text{O}_7$  or  $\text{H}_2\text{SO}_4\cdot\text{SO}_3$ . Evaluation of value depends largely on the content of  $\text{SO}_3$ . Gravimetric method is best—using Barium Chloride.—P.J. ii./12,711.

## **ACIDUM SULPHUROSUM.**

Sulphurous acid is a strong reducing agent. For example, many colours are bleached by the sulphurous acid combining with the oxygen of any water present, hydrogen being liberated, which latter forms colourless compounds with the colours. These compounds may then be removed by washing.

The gas compressed in small cylinders was used for Room Disinfection, but Formalin (*q.v.*) is more used now.

“Clayton Gas,” consisting principally of the residual nitrogen of the air, sulphurous acid up to 15%, and a considerable amount of sulphuric acid (which is useful, as it renders the gas visibly opaque) has been employed for freeing ships’ holds from vermin. A special apparatus is used.

Calcii Bisulphis. Is an antiseptic supplied in solution. Checks fermentation and putrefaction. Has been employed for preserving foods. (“Madame Rachel”).

Calcium Sulphite,  $\text{CaSO}_3 = 120.14$  I. Wts.. A white powder. soluble in dilute Sulphurous Acid, has similar properties in less degree.’

## **ACIDUM TARTARICUM.**

### **Estimation of Lead in Tartaric Acid.**

Best English tartaric acid as a rule does not contain more than 5 parts per million of lead and rarely exceeds 10. Foreign acids contain more. (*c.f.* Govt. Report *infra*).

Prepare a standard lead nitrate solution in water 0.4 Gm. in 250 Cc. This should be kept distinctly acid, and is diluted 100 times for use. 1 Cc. of this diluted solution contains 0.00001 Gm. Pb. 7 Gm. of tartaric acid are dissolved in 50 Cc. of water in a Nessler glass with internal diameter 2.5 Cm., and in another 2 Gm. of the same acid are dissolved in the same amount of water. To the first, ammonia is added in excess, and a few drops of a 10 per cent. potassium cyanide solution are added to prevent the iron and copper from interfering with the sodium sulphide solution which is then added to the first Nessler glass.

The amount of lead solution added to the ‘dummy’ to match the colour of the solution of the sample on adding sulphide is the amount present in 5 Gm. of the sample. One arrives, therefore, at the amount of lead present in parts per million; *e.g.*, 5 grammes of acid requiring 5 Cc. of diluted standard lead solution to balance coloration represent a content of 10 parts per million. Do not add lead solution after the sodium sulphide, this is a grave source of error.

To eliminate the inherent colour of the solution of the substance before adding the sulphide it may be necessary to add a minute quantity of burnt sugar to the ‘dummy.’

If the sample be rich in lead, use correspondingly less of it, *e.g.* 2 Gm.

**Method of Producing Lead-free Tartaric Acid.**—Where the proportion of lead is excessive (*e.g.* 40 parts per million), pure lead-free acid for use as ‘dummy’ will be necessary. To prepare this 250 Gm. of the best acid obtainable are placed in a strong bottle fitted with rubber cork, and 1600 Cc. cold saturated hydrogen sulphide solution are added to nearly fill the bottle, which is (cautiously) then well shaken to dissolve the acid. Great internal pressure is produced owing to comparatively slight solubility of hydrogen sulphide in solutions of citric or tartaric acid. Allow to stand one day, filter, evaporate and crystallise. The solution on concentrating may become straw-coloured, which can be removed by stirring into the hot solution a crystal of sodium chlorate. The first crop of crystals equal to half the acid taken will be absolutely lead-free.—C. Alex. Hill, C.D. March 15, 1905.



The Government Laboratories (MacFadden's Report to Local Government Board) found no Arsenic in the English Tartaric Acid and in no case more than 0.002% of lead—approximately  $\frac{1}{4}$  grain per lb. With nearly half the foreign acids this figure was exceeded—the worst being a German acid and containing 0.0062% of Metallic Lead.

Minute amounts of Lead and Arsenious Oxide below 0.002 ( $= \frac{1}{4}$  grain, per lb.), and 0.00014% ( $\frac{1}{100}$  grain per lb.) respectively, would not justify condemnation.—B.M.J. ii./07, 1140, c.f. also p. 24.

Lead should not exceed 10 to 20 parts per million.

Off. requires not exceeding the latter figure and 1.4 per million Arsenic.

C. Alex. Hill recently communicated results of 4 years' testing of this and other chemicals for Lead and Arsenic.—C.D., ii./14, 17.

**Acidum Glutaricum.** *Syn. n-* PYROTARTARIC ACID.

$\text{COOH}(\text{CH}_2)_3\text{COOH} = 132.064$ . I. Wts.

Isomeric with Methyl-Succinic, Ethyl-Malonic and Dimethyl-Malonic Acids, four isomers being possible. Colourless crystals,—soluble in water and alcohol. M.Pt. 97° C.

Experimentation by injection of dogs rendered diabetic by means of phloridzin,—showed its value in diabetes. The excretion of Nitrogen diminished. Seems to act by preventing the splitting up of the tissues, or food into sugar and urea.—B.M.J. ii./07, 542. (See also M. 1908, 114).

## ACONITI RADIX.

Off. requires not less than 0.4% Ether-soluble Alkaloids in the dried root.

Assay of aconite herb, root and extract by various methods using Iodeosin\* as indicator; also method of examining this compound for analytical purposes.—P.J. i./03, 267.

Assay experiments using the drug purposely spoilt by damp and allowed to go fungoid. Also results with old samples of the drug showed that the alkaloidal content is a distinct indication of the value corresponding with physiological test results. In the first case, *e.g.*, the alkaloidal content was 0.66% before and 0.3% approx. after spoiling. Aconite properly kept will not deteriorate. When deterioration is due to heat the weight of Ether-soluble residue is increased, the basic properties decreased, hence the deterioration is easily detected by volumetric assay. Chloroform should not be used in the assay.—P.J. ii./11, 33.

A foreign sample of root, probably containing some *A. Variegatum* had 0.53% of alkaloid—practically pure Aconitine (Freund's formula). 1 Cc. N/10 Acid (Cochineal) = 0.06406 Gm.—Evans Anal. Notes, 1912.

Farr and Wright found in Aconite Extract an average of 0.43% total alkaloid. The amount in the root is about twice that of the leaf. They found in dry root extract from 1.2 to 6%, English root being the best. A method of making the extract is outlined. The average yield of the dry extract was 25.9%, the Ether-soluble alkaloid in this averaging 1.95%. Foreign root yielded 30% with an average of only 0.68% Ether-soluble alkaloid. A standard of 1% proposed. The dose of this Extract would be  $\frac{1}{2}$  to  $\frac{1}{4}$  grain. Foreign root is very mixed owing to mode of collection.—P.J. i./13, 216; C.D. i./13, 271.

## ACONITINA.

The B.P. 1898 formula was Dunstan's original one. The Off. formula is Schulze's—*v.p.* 12. Freund's formula is  $\text{C}_{34}\text{H}_{47}\text{NO}_{11}$ . (Schmidt at Marburg now also gives Freund's formula as the most likely). Dunstan also uses it

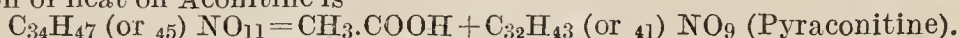
\* NOTE.—Iodeosin Test Solution, U.S. Tetra-iodofluorescein  $\text{C}_{20}\text{H}_8\text{I}_4\text{O}_5$ , 0.1% in alcohol. Becomes colourless in acid solutions, pink in alkaline. Dilute the solution to be titrated with 100 Cc. or so of water, add 20 Cc. ether and 5 drops of the indicator and shake. Titration complete when pink persistent. For alkaloidal residues dissolve in known volume standard acid, dilute 100 Cc., and proceed as above. It is very suitable for use as an indicator when titrating alkaloidal residues with Centinormal or weaker acid.—P.J. /08, 194.



for Aconitine prepared on the Continent, and suggests that the substance from English roots is a different body. Schulze says they are identical.

FR. CX. has also U.S. (Freund's) formula. Also PH. ITAL. Latter gives tests for pseudaconitine and aconine as adulterants.

Schulze and Liebner (Arch. d. Pharm., 1913, 251, p. 453) show that the action of heat on Aconitine is



Pyraconitine, according to Dunstan and Carr, was thought to have the composition  $\text{C}_{31}\text{H}_{41}\text{NO}_{10}$ . S. and L.'s examinations of the Salts of Pyraconitine (perchlorate, etc.), also confirm the above composition, and hence the new formula  $\text{C}_{34}\text{H}_{47}\text{NO}_{11}$  or  $\text{C}_{34}\text{H}_{45}\text{NO}_{11}$  for Aconitine. Pyraconitine is optically active, not inactive as stated by Dunstan.

Further work on Japaconitine (c.f., Vol. I., p. 798). shows the pyrojapaconitine produced in analogous manner by heat is identical with pyraconitine, and that japaconitine and aconitine are probably isomeric.—C.D. ii./13,656; P.J. ii./13,541.

O. L. Brady, JI. Chem. Soc., Oct. 1913, p. 1821, finds Freund's formula satisfactory, though combustion figures are equally in favour of Schulze's formula  $\text{C}_{34}\text{H}_{45}\text{O}_{11}\text{N}$ . The presence or absence of the 2H atoms will be determined when the constitutional formula is known. At present all that is certain is that it contains 4 Methoxy groups, 3 Hydroxyls, one Nitrogen-Methyl, one Acetyl and one Benzoyl group. The supposition that German Aconitine is not identical with English Aconitine cannot be founded on fact.—C.D. ii./13,706; P.J. i./14,219.

**Oxidation of Aconitine.**—In Aconitine there are 3OH, 4 O.CH<sub>3</sub> and 1 CH<sub>3</sub> groups leaving a residue  $\text{C}_{20}\text{H}_{21}\text{N}$ . On heating Aconitine Permanganate with Dilute Sulphuric Acid a body termed **Oxonitin** is produced, neither basic nor alkaloidal nor acidic. It differs from Aconitine by  $\text{C}_{10}\text{H}_{14}\text{OH}(\text{OCH}_3)$ . From Oxonitin a hydrolytic alkaloid was obtained but insufficient for further investigation.

Japaconitin also yields Oxonitin by the same method.—P.J. ii./12,619 C.D. ii./12,752.

FR. CX. gives tests for distinguishing pure aconitine from decomposition products and substances which occur with it in the root.

④ **Pseudaconitine.**—A crystalline alkaloid obtained from Indian (or Nepaul) aconite, *A. ferox*, melts at 201° C. and has the constitution of acetyl-veratryl-pseudaconine.

⑤ **Indaconitine** or Acetyl-benzoyl-pseudaconine—  
Is from *Aconitum Chasmanthum*.

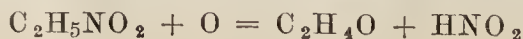
⑥ **Bikhaconitine** (crystalline) is obtained from *A. spicatum*.—L. ii./05, 1347. May be used as substitutes for aconitine and pseudaconitine for internal use, the dose in the case of the latter being  $\frac{2}{3}$  of that of aconitine.

## ÆTHERIS NITROSI SPIRITUS. (Off.).

**Estimation.**—5 Cc. of this Spirit treated with 5 Cc. of Potassium Iodide Solution and 5 Cc. of Dilute Sulphuric Acid yield at least 20 (B.P. '98 was 31 $\frac{1}{2}$ ), but not more than 25 Cc. of Nitric Oxide, corresponding to 1.52 to 2.66% by weight of Ethyl Nitrite, Iodine being liberated.

Ammonium Acetate or Citrate hinders the deterioration of Spirit of Nitrous Ether.—D. J. Leech.

This preparation kept under the best conditions undoubtedly decomposes, aldehyde and acetic and nitrous acids being among the products of decomposition. There is, besides, a certain amount of loss by evaporation of ethyl nitrite. MacEwan in 1884 showed that under the best conditions the acidity of the spirit increases on keeping as well as the aldehyde. Decomposition of ethyl nitrite is inevitable, because the preparation contains about 10 per cent. of water, so that the ethylic ester and water interact, the preparation getting into a state of incipient decomposition, which is consummated as soon as the spirit is agitated with air, as is unavoidable in repeatedly opening the bottle. The first change may be the formation of aldehyde and nitrous acid, thus :

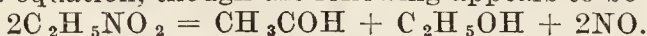


Then the aldehyde is oxidised into acetic acid.

In the course of time the nitrous constituent of the spirit entirely disappears, but aldehyde, one of the most readily oxidisable bodies, remains. It was also proved that formic acid is one of the products of decomposition of sweet spirit of nitre made from methylated spirit.

It is generally packed by the manufacturer in full bottles as soon as made, and its strength ascertained and recorded when bottled. It therefore reaches retailers practically of undiminished strength, and it is their duty to store the spirit in cool cupboards and in well-filled bottles, kept preferably upside down.—C.D. i./11,17.

With regard to the 'volatilisation' of Ethyl Nitrite, Cowley finds that every trace of Ethyl Nitrite disappears from a solution within a few days in ordinary vessels. As to decomposition in an *Aqueous Solution*, a mixture containing Spirit of Nitre loses the whole of it in three days. With regard to decomposition in *Alcoholic Solution*, this is of such varied character that it is impossible to represent by an equation, though the following appears to be preliminary :



Solutions in Absolute Alcohol change less rapidly than those in 90% Alcohol on account of the Water present.—C.D. April 15/11,556.

He advises from result of experiments a mixture of 90% Alcohol and Glycerin in equal volumes as a solvent for all preparations of Ethyl Nitrite

## ALCOHOL.

### Rule for Calculation for Dilution of Alcohol.

If **V** be volume percentage of the stronger alcohol and **v** of the alcohol required—

I. *By volume.* Mix **v** volumes of the stronger alcohol with distilled water, *q.s.*, after cooling to make **V** volumes, *e.g.* to make an alcohol 43% from alcohol 95% take 43 volumes of the 95% and make up to 95 volumes.

II. *By weight.* Proceed on same lines by weight throughout.

To Transpose Volume per cent. of Alcohol into Weight per cent. The volume per cent. is multiplied by 0.7938, and the product divided by the Sp. Gr. of the liquid, *e.g.*,  $\frac{80.22 \text{ V per cent.} \times 0.7938}{0.863} =$

73.7875 weight per cent. To express the Weight per cent. as Volume per cent. divide the weight per cent. by 0.7938 and multiply by the Sp. Gr. of the liquid, *e.g.*, 90.29 per cent. by weight =  $\frac{90.29 \times 0.822}{0.7938} = 93.49 \text{ V per cent.}$

To state Volume per cent. as Alcohol of Proof Strength. Multiply V per cent. by 1.753 and deduct 100 from the product. Thus 65 V per cent. =  $65 \times 1.753 - 100 = +13.945^\circ$  over proof. Further, alcohol of 25 V per cent. =  $25 \times 1.753 - 100 = -56.175^\circ$  proof, *i.e.*,  $56.175^\circ$  under proof.

B.P., 1885, stated: Proof spirit = about 57 per cent. alcohol ( $\text{C}_2\text{H}_5\text{OH}$ ) by vol., *i.e.*, 57 parts alcohol with water produce 100 parts proof spirit.

$\therefore$  1 part alcohol will make  $\frac{100}{57} = 1.753$  (about) parts proof strength.

Laws governing the Molecular combination of Alcohol with Water. —P.J. i./10,754.

The following Table, founded on B.P. 1898, and Gilpin's Tables shows :—

(i.) The volume of Distilled Water necessary to be added to 100 volumes of Alcohol (90%) for the production of each strength of Diluted Alcohol.

(ii.) The volumes of Alcohol (90%), and of Distilled Water respectively which, when mixed and reduced to 60° F. (15·5° C.), will produce, allowing for contraction in volume, 1,000 Ce., 1 pint, or 1 gallon of each strength of Diluted Alcohol.

The Specific Gravity and the exact Excise (Sikes') strength at 60° F. (15·5° C.), in degrees over proof (O.P.) and under proof (U.P.), of each dilution, are given in the first column.

TABLE FOR THE DILUTION OF ALCOHOL (90%) TO WEAKER (*Off.*), STRENGTHS.

Volume Percentage, Specific Gravity, and Excise Strength.	Alcohol. (90 per cent.)	Distilled Water.	Volume Produced.
70 per cent. Sp. Gr. 0·8900 22·7° O.P.†	100 vols. + 31·05 vols. 777·8 Ce. + 241·6 Ce. *648·5 Gm. + 241·6 Gm. 15 oz. 266 m. + 4 oz. 398 m. 124 oz. 215 m. + 38 oz. 307 m. *6 lbs. 7 $\frac{7}{8}$ oz. + 2 lbs. 6 $\frac{5}{8}$ oz. = 8 lbs. 14 $\frac{1}{2}$ oz.	= 128·57 = 1000Ce. = 1000Ce. = 1 pint = 1 gal.	
60 per cent. Sp. Gr. 0·9135 5·20° O.P.†	100 vols. + 53·65 vols. 666·7 Ce. + 357·8 Ce. *555·9 Gm. + 357·8 Gm. 13 oz. 160 m. + 7 oz. 74 m. 106 oz. 320 m. + 57 oz. 112 m. *5 lbs. 9 oz. + 3 lbs. 9 $\frac{1}{4}$ oz. = 9 lbs. 2 $\frac{1}{4}$ oz.	= 150 = 1000Ce. = 1000Ce. = 1 pint = 1 gal.	
45 per cent. Sp. Gr. 0·9436 21·2° U.P.†	100 vols. + 105·34 vols. 500 Ce. + 526·6 Ce. *417·2 Gm. + 526·6 Gm. 10 oz. + 10 oz. 256 m. 80 oz. + 84 oz. 130 m. *4 lbs. 2 $\frac{7}{8}$ oz. + 5 lbs. 4 $\frac{1}{4}$ oz. = 9 lbs. 7 oz.	= 200 = 1000Ce. = 1000Ce. = 1 pint = 1 gal.	
20 per cent. Sp. Gr. 0·9760 64·9° U.P.†	100 vols. + 355·8 vols. 222·2 Ce. + 790·7 Ce. *185·2 Gm. + 791 Gm. 4 oz. 213 m. + 15 oz. 390 m. 35 oz. 267 m. + 126 oz. 243 m. *1 lb. 13 $\frac{3}{4}$ oz. + 7 lbs. 14 $\frac{1}{2}$ oz. = 9 lbs. 12 $\frac{1}{4}$ oz.	= 450 = 1000Ce. = 1000Ce. = 1 pint = 1 gal.	

NOTE.—\*These figures are the weights necessary to produce a gallon and a litre respectively, at 15·5° C.—P.J. i./98,501. †Stevenson.



## ALCOHOL TABLE.

NOTE.—*Specific gravities are taken at 15.5° C.*

Sp.Gr.	Wt. per cent.	Vol. per cent.	Sp.Gr.	Wt. per cent.	Vol. per cent.	Sp.Gr.	Wt. per cent.	Vol. per cent.	Sp.Gr.	Wt. per cent.	Vol. per cent.
0.999	0.53	0.66	0.947	36.00	42.95	0.895	60.26	67.93	0.843	82.15	87.24
0.998	1.06	1.34	0.946	36.56	43.56	0.894	60.67	68.33	0.842	82.54	87.55
0.997	1.69	2.12	0.945	37.11	44.18	0.893	61.08	68.72	0.841	82.92	87.85
0.996	2.28	2.86	0.944	37.67	44.79	0.892	61.50	69.11	0.840	83.31	88.10
0.995	2.83	3.55	0.943	38.22	45.41	0.891	61.92	69.50	0.839	83.69	88.46
0.994	3.41	4.27	0.942	38.78	46.02	0.890	62.36	69.92	0.838	84.08	88.76
0.993	4.00	5.00	0.941	39.30	46.59	0.889	62.82	70.35	0.837	84.48	89.08
0.992	4.62	5.78	0.940	39.80	47.13	0.888	63.26	70.77	0.836	84.88	89.39
0.991	5.25	6.55	0.939	40.30	47.67	0.887	63.70	71.17	0.835	85.27	89.70
0.990	5.87	7.32	0.938	40.80	48.21	0.886	64.13	71.58	0.834	85.65	89.99
0.989	6.57	8.18	0.937	41.30	48.75	0.885	64.57	71.98	0.833	86.04	90.29
0.988	7.27	9.04	0.936	41.80	49.29	0.884	65.00	72.38	0.832	86.42	90.58
0.987	7.93	9.86	0.935	42.29	49.81	0.883	65.42	72.77	0.831	86.81	90.88
0.986	8.64	10.73	0.934	42.76	50.31	0.882	65.83	73.15	0.830	87.19	91.17
0.985	9.36	11.61	0.933	43.24	50.82	0.881	66.26	73.54	0.829	87.58	91.46
0.984	10.08	12.49	0.932	43.71	51.32	0.880	66.70	73.93	0.828	87.96	91.75
0.983	20.85	13.43	0.931	44.18	51.82	0.879	67.13	74.33	0.827	88.36	92.05
0.982	11.82	14.37	0.930	44.64	52.29	0.878	67.54	74.70	0.826	88.76	92.36
0.981	12.38	15.30	0.929	45.09	52.77	0.877	67.96	75.08	0.825	89.16	92.66
0.980	13.15	16.24	0.928	45.55	53.24	0.876	68.38	75.45	0.824	89.54	92.94
0.979	13.92	17.17	0.927	46.00	53.72	0.875	68.79	75.83	0.823	89.92	93.23
0.978	14.82	18.25	0.926	46.46	54.19	0.874	69.21	76.20	0.822	90.29	93.49
0.977	15.67	19.28	0.925	46.91	54.66	0.873	69.63	76.57	0.821	90.64	93.75
0.976	16.46	20.24	0.924	47.36	55.13	0.872	70.04	76.94	0.820	91.00	94.00
0.975	17.25	21.19	0.923	47.82	55.60	0.871	70.44	77.29	0.819	91.36	94.26
0.974	18.08	22.18	0.922	48.27	56.07	0.870	70.84	77.64	0.818	91.71	94.51
0.973	18.35	23.10	0.921	48.73	56.54	0.869	71.25	78.00	0.817	92.07	94.76
0.972	19.67	24.08	0.920	49.16	56.98	0.868	71.67	78.36	0.816	92.44	95.03
0.971	20.50	25.07	0.919	49.64	57.45	0.867	72.09	78.73	0.815	92.81	95.29
0.970	21.31	26.04	0.918	50.09	57.92	0.866	72.52	79.12	0.814	93.18	95.55
0.969	22.08	26.95	0.917	50.52	58.36	0.865	72.96	79.50	0.813	93.55	95.82
0.968	22.85	27.86	0.916	50.96	58.80	0.864	73.38	79.85	0.812	93.93	96.08
0.967	23.62	28.77	0.915	51.38	59.22	0.863	73.79	80.22	0.811	94.28	96.32
0.966	24.38	29.67	0.914	51.79	59.63	0.862	74.23	80.60	0.810	94.62	96.55
0.965	25.14	30.57	0.913	52.23	60.07	0.861	74.68	81.00	0.809	94.97	96.78
0.964	25.86	31.40	0.912	52.68	60.52	0.860	75.14	81.40	0.808	95.32	97.02
0.963	26.53	32.19	0.911	53.13	60.97	0.859	75.59	81.80	0.807	95.68	97.27
0.962	27.21	32.98	0.910	53.57	61.40	0.858	76.04	82.19	0.806	96.03	97.51
0.961	27.93	33.81	0.909	54.00	61.84	0.857	76.48	82.54	0.805	96.37	97.73
0.960	28.56	34.54	0.908	54.48	62.31	0.856	76.88	82.90	0.804	96.70	97.94
0.959	29.20	35.28	0.907	54.95	62.79	0.855	77.29	83.25	0.803	97.03	98.16
0.958	29.87	36.04	0.906	55.41	63.24	0.854	77.71	83.60	0.802	97.37	98.37
0.957	30.44	36.70	0.905	55.86	63.69	0.853	78.12	83.94	0.801	97.70	98.59
0.956	31.00	37.34	0.904	56.32	64.14	0.852	78.52	84.27	0.800	98.03	98.80
0.955	31.62	38.04	0.903	56.77	64.58	0.851	78.92	84.60	0.799	98.34	98.98
0.954	32.25	38.75	0.902	57.21	65.01	0.850	79.32	84.93	0.798	98.66	99.16
0.953	32.87	39.47	0.901	57.63	65.41	0.849	79.72	85.26	0.797	98.96	99.35
0.952	33.47	40.14	0.900	58.05	65.81	0.848	80.13	85.59	0.796	99.29	99.55
0.951	34.05	40.79	0.899	58.50	66.25	0.847	80.54	85.94	0.795	99.61	99.75
0.950	34.52	41.32	0.898	58.95	66.69	0.846	80.96	86.28	0.794	99.94	99.86
0.949	35.00	41.84	0.897	59.39	67.11	0.845	81.36	86.61	0.7938	100.00	100.00
0.948	35.50	42.40	0.896	59.83	67.53	0.844	81.76	86.93			

Based on figures of  
O. Hehner

**Detection of Methyl Alcohol.**—Place in a 100 Cc. Erlenmeyer flask, as a check, Sodium Salicylate 0.5 Gm. and pure Alcohol 1 Cc., and into a similar flask Sodium Salicylate 0.5 Gm. and 1 Cc. of the Spirit to be tested. To both flasks add twenty drops of Sulphuric Acid in four parts at an interval of one minute. If Methyl Alcohol is present, an odour of Methyl Salicylate is developed. On adding an emulsion of quick lime 0.4 Gm. in 2 Cc. Sodium

Hydrate Solution, an odour like Phenyl-Methyl-Ether is developed after a minute.—Sailer, Pharm. Zeit., 1912, 57, 93; J.C.S.A. ii./12,301; see also P.J. ii./05,440. Tests and Trade varieties.—P.J. i./07,404.

“**Proof Spirit**” has Sp. Gr. 0.920. This, in the olden time, was found to be the weakest spirit that could be put to the proof of igniting a little gunpowder moistened with it. If the spirit caught fire and inflamed the gunpowder, it was designated “over proof,” and if not, “under proof.” By the Hydrometer Act, 58 Geo. III. Cap 28, Proof Spirit is defined as spirit of strength, which at a temperature of 51° F. weighs exactly twelve-thirteenths of an equal quantity of distilled water.

### Spiritus, P.G.V.

Aldehyde tests (P.G.V.) The red colour of a mixture of 10 Cc. of alcohol and 1 Cc. of potassium permanganate solution (1+999) should not turn to yellow within twenty minutes. On adding to a mixture of 10 Cc. of spirit, 10 Cc. of water, and 1 Cc. of silver nitrate solution (1+19), sufficient solution of ammonia to redissolve the precipitate at first thrown out, and then placing the mixture in the dark, no colouration or opalescence should occur within five minutes.

### AMOUNT OF ETHYLIC ALCOHOL BY VOLUME IN VARIOUS LIQUORS.

Whisky ... ..	White Wine ... ..	12 - 14%
Rum ... ..	Champagne ... ..	10 - 13%
Gin ... ..	Orange Wine ... ..	10 - 12%
Strong Liqueurs ... ..	Burgundy ... ..	9 - 12%
Proof Spirit ... ..	Hock ... ..	9 - 12%
Brandy ... ..	Claret ... ..	8 - 12%
Port ... ..	Cider ... ..	5 - 9%
White Wine (strong) ... ..	Strong Ale or Stout ... ..	5 - 9%
Sherry ... ..	Beer and Porter ... ..	2 - 5%
Madeira ... ..		

HALE WHITE.

Special Analytical Commission on Whisky and details of Manufacture.—The Hospital, Apl. 7,06, p. 8.

P. Helv. gives a useful summary of analysis of wines.

Alcoholic fermentation. Presence of Phosphorus (Phosphate) essential. (International Chemical Congress Paper) B.M.J. i./09,1375.

Suitable amounts of an Arsenate added to yeast juice increase rate of fermentation.—Na, Mar., 1911, 65.

Beer—Materials and substitutes used in making.—B.M.J. i./09,673.

Alcohol without fermentation.—Some experimental attempts to de-alcoholise beer without altering its flavour, keeping qualities or aeration by the simple process of driving CO<sub>2</sub> into it, showed that it was possible to reduce the alcohol percentage to 0.2% at 120° F. On freezing and further treatment by the CO<sub>2</sub> the content rose to 1.16. Further experiments, however, not completely in accord.—P.J. i./11,30.

Royal Commission on Whisky and other Potable Spirits, Definitions of Brandies, Rum, Gin, etc.—B.M.J. ii./09,399.

Bonded Warehouses and Spirits in Bond.—C.D. ii./06,510.

Lancet report on Cognac brandy.—L. ii./03,1503.

Some 40 or 50 abstracts of Patents and references to the production of Alcohol from materials other than the usual maize, potatoes, molasses, e.g., bananas, apple juice, chicory roots, peat, straw, currants, oil cake, etc., were found in the J.S.C.I., between 1893 to 1911. A trial factory in U.S.A., is said to be producing 78 litres of Absolute Alcohol from one ton of dry sawdust (from one ton of potatoes 20 litres can be obtained). Sulphite Cellulose waste products said to be even more productive. The principle involved is the conversion of the cellulose into fermentable sugars.—Thomas Tyrer, —B. & C.D., May 26/11,452; L. ii./10,1924.

In the **Classen Process** for Alcohol production sawdust is digested with weak Sulphurous Acid in an autoclave under 90 to 100 lbs. pressure, yielding a product containing 25% of sugar, 18% alkali or acid-soluble, and 56% insoluble carbol hydrates. The solid Saccharine residue is a suitable spirit making material, but the Spirits Act, 1880, places such restrictions on the Spirit Industry as to stop the process.



A factory capable of treating 200 tons of sawdust per week could turn out between 300,000 and 400,000 gals. of proof spirit per annum. This would also give by-products of 50 tons acetic acid, 10 tons furfural, and 2,000 gals. of methyl alcohol for recovery. The spirit produced is of high quality, being free from fusel oil.—A. Zimmermann, C.D., Dec. 7/12.

For preservation of natural history specimens biologists might well make use of antiseptics instead of Alcohol and Methylated Spirit.—P.J. i./11,768.

**Excise Duty on spirit** was advanced in 1909 by 3/9 per proof gallon; it was previously 11/- per gallon proof. This duty (14/9), remains the same.—1914. (Proof spirit is approximately alcohol 50%.—*c.f. antea.*)

**'Duty Free' Alcohol** for Chemical Industries. Current position of.—P.J. ii./14,316,339.

The regulations governing the use of Industrial Spirit are prescribed by the Commissioners of Inland Revenue under Authority of the Spirits Acts, 1880. Iodine in Industrial Spirit not permitted.—B.M.J. i./14,1200.

**Ethyl Butyrate.**— $C_3H_7.COO.C_2H_5 = 116.096$  I. Wts. The chief constituent of Pine Apple Essence. A colourless liquid with Pine Apple odour. Sp. Gr. 0.886 @ 15° C. Miscible with Alcohol. Boiling about 120° C.

**Iso-Amyl Butyrate.**

$CH_3.CH_2.CH_2.COO.CH_2.CH_2.CH_3 = 158.144$  I. Wts.

Colourless liquid with Sp. Gr. 0.882 @ 0° C. Used as a flavouring agent.

## ALDEHYDUM FORMICUM.

### *Formalin as Preservative :—*

By the **Linley Process** meat is sterilised by placing in "Chilling Rooms" and then to every cubic foot of space in the chamber at 50° to 60° F. a fan distributes 1 ounce of Formalin. This acts on the meat, which is finally frozen for shipment at 32° F.

The Local Government Board issued a report by Buchanan and Schryver on use of Formaldehyde and Paraform for meat preservation. Of the former a mixture of Glycerin, Salt and Formalin is used. Paraform is volatilised in shipholds to kill mould not stopped by the cold. Can be detected in the meat. Recommendation to limit use to sanitary disinfection before meat is introduced.—C.D. ii./09,343.

The process remains under careful observation and in present circumstances it does not seem necessary to take steps to prohibit its use.—L. i./10, 833.

For Milk, etc., see Milk Analysis, pp. 270, 271.

**Determination of Formaldehyde**—4 to 4½ Gm. of the solution (if about 40%) is accurately weighed into a stoppered flask of 150 to 200 Cc., about 50 Gm. of Ammonium Chloride in fine powder are next added and then 25 Cc. of a double Normal Solution of Caustic Soda,—flask is shaken meanwhile. Contents and flask are allowed to cool down to temperature of room, then 50 Cc. of Water, containing 4 drops of 1% Solution of Methyl Orange are added and titrated with Normal Sulphuric Acid. The number of Cc. of Normal Soda used, multiplied by 0.06 gives the weight of Formaldehyde. If the solution be acid another portion is titrated with decinormal alkali and phenolphthalein and the necessary correction made in the amount of Soda neutralised.—P.J. i./11,433. Other methods P.J. ii./08,840 (Colorimetric), ii./10,637,881. Am. Jl. Ph., Oct. 1911, 455; *c.f.* also Estimation in Saponaceous Solutions, *infra*.

**U.S. Method of Estimation** is as follows :—

Weigh about 3 Gm. into a stoppered Erlenmeyer flask, add 50 Cc. N/1 Sodium Hydrate Solution, then add gradually through a small funnel 50 Cc. of Hydrogen Peroxide 10 volume strength (previously neutralised to litmus). Allow to stand 10 minutes and titrate with N/1 Sulphuric Acid using litmus as indicator. Multiply the number of Cc. of N/1 Sodium Hydrate used by the Formic Acid produced from the Formalin by 3.0016 and divide by the weight of the Formalin taken. This will give the percentage of Formaldehyde present. *Off.* method is similar.

**P. G. Method** depends on reaction between Formaldehyde and Neutral Sodium Sulphite. The Bisulphite compound is formed and the Sodium

Hydrate liberated is titrated with N/1  $\text{H}_2\text{SO}_4$  using Phenolphthalein as indicator:—



C. H. Hampshire and S. Furnival modified the P.G. process slightly as follows.—To 50 Cc. of freshly made Sodium Sulphite Solution (P.G. uses  $12\frac{1}{2}$  Gm. of the crystalline salt in 50 Cc. of water), add a little Phenolphthalein and make solution colourless by carefully adding N. Sulphuric Acid. 1 Cc. of the Formaldehyde is then added and the mixture titrated at once with N/1  $\text{H}_2\text{SO}_4$  until the colour completely disappears. 1 Cc. of Acid = 0.030016 Gm. HCOH.

They examined 11 samples of Formaldehyde Solution of commerce and found specific gravity to vary from 1.0804 to 1.0886.

H.CO.H by weight 35.38% to 37.33% ; average 36.56%.

$\text{CH}_3\text{OH}$  by weight 10.16% to 14.97% ; average 13.68%.

Presence of Methyl Alcohol prevents polymerisation but renders the solution liable to duty on basis of Ethyl Alcohol.

**Formaldehyde Tablets** containing usually  $\frac{1}{8}$  grain with Lactose, were found deficient. Estimation process by steam distillation.—P.J. ii./12, 133,174.

## ALOES.

### Extract Content in Aloes.

We obtained recently (1914) the following figures from 10 samples of Aloes—5 Socotrine and 5 Barbados.

Aloes Barbados	1.	2.	3.	4.	5.
Soluble in cold water .	61.1%	62.0%	73.5%	69.6%	58.0%
Insoluble residue ..	30.0%	29.7%	16.6%	20.5%	31.5%
Aloes Socotrine	1.	2.	3.	4.	5.
Soluble .. ..	49.2%	50.4%	51.0%	35.4%	49.2%
Insoluble .. ..	40.7%	40.4%	39.5%	53.8%	40.3%

The process was as follows—5 Gm. of Aloes in powder triturated with water 50 Cc. transferred to a counterbalanced filter paper and washed with sufficient water to make filtrate up to 200 Cc. An aliquot part (50 Cc.) was evaporated on the water bath and the residue dried for one hour at  $110^\circ \text{C}.$ , the residue on the filter paper being pressed and dried at  $110^\circ \text{C}.$  for two hours. To obtain concordant results it is necessary to use the same volume of water. A figure for insoluble residue is not of much use alone as it does not give the soluble matter by difference owing to the amount of moisture present in the sample which is variable and accounts for the difference between the above figures and 100.

*Off.* requires loss on drying not more than 10%.

**Tests for different varieties of Aloes**, see Allen, 1913, Vol. VII., p. 146. Tests for Adulterants *ibid.*, p. 138.

**Anthraquinone derivatives** other than Aloe-Emodin, Investigation to determine presence of. The results were negative. Aloe-Emodin was extracted by Petroleum Ether after distilling off an Essential Oil with steam. Both Cinnamic and *p*-Coumaric Acids were also obtained from the Aloes.—F. Tutin and W. J. S. Naunton, P.J. ii./13,836.

### Characters and Tests of Aloin.

0.01 Gm. dissolved in 5 Cc. Water, 1 drop of Copper Sulphate Solution added and the mixture warmed, a red colour is produced—too much Copper spoils the colour.

The dry substance gives red colour with strong  $\text{HNO}_3$ , but Aloin from Cape Aloes gives green. An aqueous solution shaken with Ether and the Ether layer separated and shaken with a little Caustic Potash, the latter becomes red—due to the small quantity of Oxymethylantraquinone present in Aloin.—P.J. ii./10,235.

## AMMONIUM.

### Spiritus Ammoniae Aromaticus.

Method of analysis and a suggestion for a change in the formula, ammonium bicarbonate recommended to take the place of the ammonium carbonate.—Am. Jl. Ph., Jan. 1912, p. 7.

Composition of,—P.J. i./12,4.



**Ammonii Sulphocyanidum.** *Syn.* AMMONII RHODANIDUM.— $\text{NH}_4\text{CNS}=76.122$  I. Wts. White crystals soluble in Water and Alcohol. Reagent in toxicology to separate Arsenic, Antimony, Mercury, etc. (Merck). Recovery after taking 30 Gm. of pure Ammonium Sulphocyanide in 200 Cc. of Water.—P.J. i./12,10.

**Hydrazine.** *Syn.* DIAMIDE  $(\text{NH}_2)_2=32.052$  I. Wts. In the basic condition this body is not stable, but the Sulphate  $(\text{NH}_2)_2 \cdot \text{H}_2\text{SO}_4$  is a well defined stable salt,—white crystals soluble in hot water. It is a useful reducing agent, *e.g.*, in making Colloidal Metal Hydrosols. It has antiseptic properties, *e.g.*, it will destroy fungi, etc.

*Photographic use.*—Recently Caldwell discovered that the inclusion of the salts of Hydrazine, or Hydroxylamine, in the emulsion renders a plate practically proof against over exposure or reversal. *Plates or papers treated with the Hydrazine Salts may also be printed right out and toned like ordinary (P.O.P.), or partly printed and the operation completed by development, and in every case a photograph of extremely fine grain and with the most perfect gradation is obtained.*—C.D.

### AMYGDALA AMARA.

#### OLEUM AMYGDALÆ ESSENTIALE.

In commerce in America Benzaldehyde is largely substituted for Oil of Bitter Almonds. Frequently Hydrocyanic Acid in sufficient quantity is added to meet the requirements of the trade or the U.S.P. Sp. Gr. should not be lower than 1.045 to 1.07 at 15° C.; *e.g.*, a sample gave gravity 1.075, containing 6.44% HCN. A pure oil requires 1 to 2 parts of 70% alcohol for solution. As to chlorinated compounds: It is becoming possible to produce Benzaldehyde showing absence of chlorine compounds. However, the presence of chlorine is strong indication of substitution. Value of copper and silver nitrate tests carefully discussed. Benzaldehyde estimation: Sodium sulphite combination in the cold, with the aldehyde and the determination of the alkali liberated does not give concordant results.—Am. Jl. Ph. Apl.'08,154.

### AQUA LAUROCERASI.

The method of preparation in the Fr. Cx. is impracticable. The Fr. Cx. assumes a content of 0.12 to 0.16% HCN in the leaves. They never yield 0.10%. The previous Fr. Cx. formula was only  $\frac{1}{2}$  this strength, viz., 0.05%.

The bright green young *Prunus Laurocerasus* leaves were found to yield from two to four times the amount of Hydrocyanic Acid given by the older and more leathery brown leaves of cherry laurel. Adequate manuring caused increase in the amount of Hydrocyanic Acid contained.—D. H. Wester, P.J. i./14,643. Ber. Deutsch. Ph. Ges. 1914,129.

**Test to distinguish Artificial Aqua Laurocerasi** (made from Benzaldehyde, Hydrocyanic Acid and Water) from the genuine. Add a few drops of Congo Red solution to a few Cc. Bright red colour with the genuine, bluish or violet tint with artificial; Benzaldehyde owing to traces of Benzoic Acid acts on the Congo Red like an acid.—P.J. ii./10,438.

### AMYL NITRIS.

Tested by means of Allen's Nitrometer, a 5% solution in alcohol should yield not less than 7.9 times its volume of nitric oxide (*Off.*).

*Our experiments show that this Standard is readily attainable, but it is important to observe that the yield of gas will vary from one experiment to another whilst using samples from the same (freshly made) Alcoholic Solution. This we believe, is due to slight differences of working—the amount of shaking in the nitrometer, etc. Actual figures for example, in one set of experiments (1914) were 7, 7.3, 7.6, 8, 8.2 and 8.5. As the errors cannot be in the negative direction, it is imperative to take highest readings when reporting upon a sample.*

P. Jap allows 0.6% acidity calculated as  $\text{HNO}_2$ , *i.e.*, 5 Cc. shaken with 0.1 Cc. of Ammonia Solution 10% and 1 Cc. water—the water must not be acid. Our examination of Amyl Nitrite by the test showed considerably less than this. U.S. allows slightly over 1% acidity, which is too large an allowance.

P.G. Test (for free Acid) is similar to P. Jap. It must not become turbid on cooling to  $0^{\circ}$  C. (absence of water).

Wilbert (Am. Jl. Ph., Sept., 1906, 413) criticises U.S. monograph and says should read 'should assay at least 80% by the process given and at the same time 80% or more of the total volume should distil between  $90$  and  $100^{\circ}$  C.'

**P. Helv. and P.G.** give test for Valerianic Aldehyde in,—1 Cc. warmed with 3 Cc. of a mixture of equal parts of Alcohol and Silver Nitrate and a few drops of Ammonia: must not blacken.

**Amyl Nitrate.**  $C_5H_{11}NO_3=133.098$  I. Wts.

Colourless liquid, Sp. Gr. 0.999. Not used to any extent in medicine.

**Amyl Acetate.** *Syn.* ISO—AMYL ACETATE,— $C_5H_{11}.CH_3COO=130.112$  I. Wts.

**PEAR ESSENCE.**—Made by action of glacial acetic acid on amylic alcohol in presence of a little sulphuric acid. Colourless Liquid. Miscible with alcohol and ether Sp. Gr. 0.876. B. Pt. about  $138^{\circ}$  C. Is used to dissolve resins in varnish making and in preparation of Collodions.

Commercial Amyl Acetate contains some of the other isomerides. As 8 isomers of Amyl Alcohol exist the acetate will vary considerably in different preparations. The iso-amyl form is generally present in dominant amount.—Thorpe's Dictionary and Allen, 1909, Vol. I., p. 249.

## ANTIMONIUM.

Determination of Antimony in fæces, etc.—The specimen is extracted with hot dilute Hydrochloric Acid, the filtrate saturated with  $H_2S$  and heated, ppt. is collected, washed and dried, evaporated with fuming  $HNO_3$  and weighed as  $Sb_2O_4$ .—P.J. ii./10,417,630; i./11,621.

The latter reference is to a colorimetric method for minute quantities in food stuffs, etc.

Antimony, Ores and Reguls (Chinese). In the assay of crude Antimony it was observed that the Antimony slightly exceeded in amount that required by formula  $Sb_2S_3$ . Deficiency of Sulphur probably owing to presence of Oxide.—P.J. i./13,337.

**Antimonii Chloridum,**  $SbCl_3=226.58$  I. Wts.

In colourless crystals. It is very corrosive and hygroscopic, hence **Butter of Antimony** used in veterinary practice is usually liquid; on addition to water, it decomposes into free hydrochloric acid and basic antimony oxychloride, powder of Algaroth; but is soluble in alcohol and carbon bisulphide.

**Liquor Antimonii Chloridi.** B.P. 1885.

A caustic liquid of reddish colour (due to iron as impurity) Sp. Gr. 1.47.

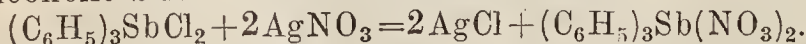
**Antimonium Sulphuratum (Off.).**

Estimation process. Oxidation with Sodium Peroxide, reduction and ultimate titration with Standard Iodine Solution. The antimony content should never be less than 30%.—P.J. ii./09,143.

## ORGANIC ANTIMONY COMPOUNDS.

G. T. Morgan, Micklethwait and Whitby communicated a paper on the Organic Antimony derivatives.—Tri-camphoryl Stibine Chloride and Triphenyl Stibine Hydroxy-nitrate and Hydroxy-sulphate. Sodium Camphor and Antimony Trichloride in dry Toluene do not interact on lines analogous with the corresponding Arsenic reaction.

Triphenyl Stibine Chloride  $(C_6H_5)_3SbCl_2$  (made by interaction of Chloro-benzene, Antimony Trichloride and Sodium), treated with Alcoholic Silver Nitrate loses its Chlorine:—



The Triphenyl Stibine Nitrate formed undergoes however partial hydrolysis forming the Hydroxynitrate  $(C_6H_5)_3Sb(OH).NO_3$ . If Silver Sulphate be used instead of the Nitrate, the Hydroxysulphate



$(C_6H_5)_3Sb(OH)SO_4.Sb(OH)(C_6H_5)_3$  is formed. It is less soluble in water than the Hydroxynitrate. It is suggested that one or other of these compounds may be suitable for use therapeutically.—J.C.S.T., Jan., 1910, p. 34.

Continuing the above work the authors report :—

Triphenyl-stibine Oxide has been obtained by hydrolysis of the Triphenyl-stibine Chloride (above), also a nitro-derivative of Triphenyl-stibine, melting at  $190^\circ$ , from this by reduction, a diazotisable amine. Some of the Acyl derivatives of this base have been prepared. By the nitration of Triphenylstibine Hydroxynitrate, a trinitro-compound is produced, which on reduction yields a crystallisable triamine, furnishing a crystalline Hydrochloride. This base has also given Acetyl and Azo- $\beta$ -Naphthol derivatives, together with platini- and stanni-chlorides.

The sulphonation of Triphenylstibine and Triphenylstibine Hydroxy-Sulphate has been undertaken, and a soluble Trisulphonic Acid obtained, yielding very soluble alkali salts.—J.C.S.P., 1910, 151.

Dr. Morgan supplied us with the following compounds for trial, the results of which may be briefly recorded:—

(A) A complex Antimonic Benzene-sulphonate containing 22.3% Sb.

(B) A solution of Sodium Triphenyl Stibine Oxide-trisulphonate O: Sb  $(C_6H_4SO_3Na)_3$

(C) A further Antimony Aryl Sulphonate containing 7% Antimony, but more complex than (A) and occurring only sometimes as a bye-product.

#### Experiments on Guinea-pigs.

The substance "A" was dissolved in water with the necessary amount of Soda, making a 5% solution. "B" and "C" were also used in 5% solution. Doses of  $\frac{1}{2}$  Cc. of each ( $=0.025$  Gm.) were tolerated. Two days later 1 Cc. of each ( $=0.05$  Gm.) were injected into the respective animals with the result that after two days the dose of "A" killed the animal. In the case of the animal which had the dose of "B" and which was the heaviest of the three animals, the effect was very marked and the animal did not recover. "C" on the other hand was completely tolerated.

Taking the fact that 0.025 Gm. of each were tolerated—this means the equivalent of a dose of over 150 grains per 12 stone man.

It is known that sulphonates are in many cases almost too non-toxic. The substance "A" was found, however, to be useless against trypanosomes.

Triamino-triphenyl Stibine Oxide and compounds of same were active against trypanosomes, but preliminary trials of the Hydrochlorides *in vivo* suggest that they are irritant when introduced subcutaneously.

G. T. Morgan has also prepared a body giving analytical data corresponding with  $NH_2.C_6H_4.Sb=Sb.C_6H_4.NH_2$ . This body, it will be noted, has the Antimony in the molecule attached to the aromatic nuclei in the same manner as is seen in the case of the Arsenic in "Salvarsan."

May,—Pr. Chem. Soc. 26 (1910) 142, J.C.S. 97, 1910, 1956, working also on Organic Antimony Compounds, gives a paper of which the following is a brief abstract:—Triphenyl Stibine Dihydroxide  $(C_6H_5)_3Sb(OH)_2$  is amphoteric in character. Experiments undertaken to observe the effect of the introduction of a  $NO_2$  group on the relative stability of the various compounds such as  $R_3SbCl_2, R_3Sb$



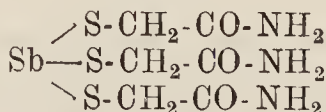
(OH)<sub>2</sub>, R<sub>3</sub>Sb(NO<sub>3</sub>)<sub>2</sub>. Triphenyl Stibine Sulphate (C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>SbSO<sub>4</sub> was made. Permanganate and dilute H<sub>2</sub>SO<sub>4</sub> oxidise Triphenyl Stibine to the Hydroxide (C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>Sb(OH)<sub>2</sub>. Alkaline Permanganate gives a better yield. The introduction of the NO<sub>2</sub> group into the Benzene nuclei of R<sub>3</sub>Sb(OH)<sub>2</sub> reduces the salt forming power of the molecule and lowers its stability as a whole.

Breinl and Nierenstein (Ann. Trop. Med. and Parasitology 1909, 2, 365), stated they had prepared *p*- and *m*-Aminophenyl Stibinic Acids H<sub>2</sub>N.C<sub>6</sub>H<sub>4</sub>.SbO(OH)<sub>2</sub> by action of Antimony Trichloride on Anilin. The Sodium Salt of this body would be the Antimony analogue of "Arsamin," but we understand this requires confirmation. Percy May, for example, states that when Antimony Chloride and Anilin react, the only organic compounds obtained contain three aromatic residues to one atom of Antimony—and compounds such as *p*-Amino-Phenyl-dichloro-stibine NH<sub>2</sub>.C<sub>6</sub>H<sub>4</sub>.SbCl<sub>2</sub> which might yield *p*-Amino-Phenyl-Stibinic Acid NH<sub>2</sub>.C<sub>6</sub>H<sub>4</sub>.SbO<sub>3</sub>H<sub>2</sub> by hydrolysis and oxidation do not appear to be formed. Sb.Cl<sub>3</sub>(C<sub>6</sub>H<sub>5</sub>.NH<sub>2</sub>)<sub>3</sub>.2HCl has been formed by heating Anilin and Antimony Trichloride. It decomposes into SbCl<sub>3</sub> and Anilin HCl on warming with HCl.—J.C.S.T., 1911, 1382.

Morgan and Micklethwait and also P. May have prepared *m*-Nitrophenylstibinic Acid NO<sub>2</sub>.C<sub>6</sub>H<sub>4</sub>.SbO(OH)<sub>2</sub>. On reduction this acid yields *m*-Aminophenyl-stibine Oxide NH<sub>2</sub>.C<sub>6</sub>H<sub>4</sub>.SbO and from this compound indications have been obtained of the production in small amount of *m*-aminophenyl-stibinic acid, the analogue of atoxyl, but containing its substituents in the meta-positions with respect to one another. Morgan and Micklethwait have also prepared di-*m*-nitrodiphenylstibinic acid (NO<sub>2</sub>.C<sub>6</sub>H<sub>4</sub>)<sub>2</sub>.SbO.OH, a substance which on reduction yields di-*m*-aminodiphenyl-hydroxystibine (NH<sub>2</sub>.C<sub>6</sub>H<sub>4</sub>)<sub>2</sub>.Sb.OH, and di-*m*-aminodiphenylstibine chloride hydrochloride Sb.Cl(C<sub>6</sub>H<sub>4</sub>.NH<sub>2</sub>)<sub>2</sub>.2HCl. Both the base and hydrochloride have an irritating action on the mucous membrane of throat and nose which is even more intense than that of tri-*m*-amino-triphenylstibine and its salts.—*vide* J.C.S.T. 1911, 2294, J.C.S.P. 1912, pp. 5 and 19.

Sodium Antimony di-Thioglycollate Sb  $\begin{matrix} \text{S-CH}_2\text{COONa} \\ \text{S-CH}_2\text{CO-O} \end{matrix}$  and the

Triamide of Antimony Tri-Thioglycollic Acid



have been tried on experimental trypanosomiasis in rats, dogs and rabbits.—Jl. Pharmac., Baltimore, 2nd October, 1910, 101–144. The results of the treatment appear to be as good as any hitherto recorded. P. May gives extracts of these papers.

The triamide is said to be well adapted for subcutaneous or intravenous use.

The injection of either of these two Antimony preparations at the time of the inoculation of the trypanosomes afforded complete pro-

tection. The Thioglycollate injected within the first 24 hours after inoculation also gave complete protection. A trial of these bodies in human trypanosomiasis is thought justified.—v. also M.A. 1911, 9.

Dosage and toxicity of Antimony compounds depends mainly on the presence of the trivalent Sb. atom, the pentavalent being less active. Organic Antimony bodies are found in both groups.—P.J. ii./12,160.

For a masterful recent paper on Organic Arsenic and Antimony Compounds by G. T. Morgan, see P.J. i./14,537,567.

*For further Organic Antimony Compounds, see Vol. I.*

## ARGENTUM.

### Argentific Hair Dye (Black or Brown).

No. 1 Solution.—Silver Nitrate 1, Distilled Water to 12.

No. 2 Solution.—Sulphurated Potash 1, Distilled Water to 8. After washing and drying the hair, the solutions to be applied separately, in above order, and after 2 minutes the hair well washed with soft water. This dyes brownish black with one application, but lighter shades may be obtained by using a weaker strength of No. 1 solution, which should not be allowed to touch the skin.

### Pyrogallol Hair Dye (Black).

No. 1 Solution.—Pyrogallol Acid 1, Alcohol (90%) 8, Distilled Water 40. Apply before No. 2.

No. 2 Solution.—Silver Nitrate 1, Strong Solution of Ammonia 1, Distilled Water to 8. Use as last.

This dyes grey hair *jet black* with one application.

Various other formulæ for "**Silver Hair Dyes**"—modifications of the above, *e.g.*, using a small addition of Sodium Meta-bisulphite in the No. 1 solution have been tried producing analogous result, but the difficulty about these preparations is that they simultaneously stain the *skin*.

### Copper Pyro Hair Dyes (Odourless).

LIGHT BROWN.—Cupric Chloride ( $\text{CuCl}_2 + 2\text{H}_2\text{O}$ ) and Pyrogallol of each 1, Water 100.

DARK BROWN.—Cupric Chloride 1, Ferric Chloride 0.5, Pyrogallol 1.5, Water 100.

BLACK.—Cupric Chloride 0.6, Ferric Chloride 2, Pyrogallol 2, Water 100. This produces a fairly natural tint.

**Amidol Hair Dye (Black).** Amidol, 80 grains. Sodium Sulphite 120 grains. Alcohol 10%, 1 ounce.

A large number of experiments conducted, April, 1911, to determine the best *black die that shall not stain the skin* showed that this Amidol formula stands first. With this dye the colour develops gradually, the excess of the solution dabbed on in the ordinary way can be slightly washed out, leaving the hair dark brown, but to produce a black, several successive applications may be necessary. In our experiments we find that grey hair so dyed will stand vigorous washing with soap and water without appreciably affecting the colour.

*It will not stain the skin* if carefully applied. It did not appear to rot the hair. The freer the hair is from grease—even the natural grease of the scalp—the quicker the action. A difficulty with regard to the solution is that it deposits the colouring on the side of the bottle.

The Amidol Dye is based on the formula in Pharm. Formulas, being double strength of the latter. The ordinary strength of Pharm. Form. gives a brown stain as stated. It has the advantage of being odorless and a *one* solution dye.

Next in order of merit in our opinion, came the "Argentific." It does not stain the skin if washed off soon after the dye has been employed.

The sale of Hair Dyes containing colours injurious to health is prohibited in Germany, *e.g.*, those colouring substances or dyes containing Antimony, Arsenic, Barium, Lead, Cadmium, Chromium, Copper, Mercury, Uranium, Zinc, Tin, Gamboge, Coraline, or Picric Acid. Hair colouring which contains



substances such as Paraphenylenediamine, Silver (except as Chloride) may be sold only in stores by persons authorised to deal in poisons. Cosmetic articles, when entering into trade as articles of healing, containing strong medicaments, or Creosote, Phenyl-salicylic Acid or Resorcin may only be sold in drug stores.—B. and C.D. i./13, p. 358.

## ARSENICUM.

**Horticultural Use.**—Method of applying wash, spray, and paste.—P.J. ii./08,722.

**Detection of Arsenic in Drugs.**—The Pharmacopœia Committee of the General Medical Council recommended the following method.

A solution of 4 Gm. of the drug is to be prepared as described in a series of special notes, and is to be diluted with water to a volume of 25 Cc. This solution is to be placed in a test tube of about three-quarters of an inch (about 2 Cm.) in diameter and 7 inches to 8 inches (18 to 20 Cm.) in length. Fragments of **granulated zinc** are to be put into the test tube until they reach to about two-thirds of the height of the liquid. Immediately after adding the zinc a small plug of cotton-wool is to be placed in the test tube above the liquid, and then a plug of **plumbised cotton-wool** so as to leave a short space between the two plugs, and a closely fitting cap formed of two mercurialised test papers to be fastened on: it must not be torn at all when fastened on the test tube. The test is to be allowed to continue for two hours at least, and the test paper is to be examined by daylight for a yellow stain. The test should be conducted in a place protected from strong light. It is applicable both in the case of arsenious and arsenic compounds.

**Arsenic in Chemicals, C.R. Supplementary Report.** Directions are given for preparing a 'standard stain' representing 1/100 mgr. of Arsenious Oxide. 109 substances are to be tested—for the majority 2 or 5 parts per million is the limit.—B.M.J. ii./12,329. An examination of the 1914 B.P. shows that 91 are so tested. **For further details see Appendix.—Off.**

**Limit of Arsenical Contamination.**—3 parts per million is an adequate limit for drugs given in small doses. It is equivalent to  $\frac{1}{35}$  grain white arsenic per pound.  $\frac{1}{100}$  grain of arsenious oxide per pound, *i.e.*, 1.08 of arsenium per million, is a reasonable limit for tartaric and citric acids, which are largely used in foods and drinks, *c.f.*, also p. 11.

This limit is confirmed by McFadden's Report to Local Government Board.—B.M.J. ii./07,1140.

In sulphuric, nitric and hydrochloric acids the limit of  $\frac{1}{16}$ ths of one part per million of arsenium is recommended, and for solution of ammonia so small a content as  $\frac{1}{16}$  is attainable.—P.J. ii./04,373, 424, 807; C.D. ii./04,434.

**Bettendorf's Reagent** for arsenic is a concentrated solution of stannous chloride in hydrochloric acid. A colourless arsenical solution will deposit brown metallic arsenic in the cold or on warming.

**Gutzeit's Test.** The substance to be examined is placed in a test tube with some arsenic-free zinc and sulphuric acid. The tube is plugged with cotton wool, and covered with filter paper having a spot of silver nitrate solution. A yellowish stain resulting in a few minutes indicates presence of arsenic. A control with lead acetate paper should be conducted to obviate confusion with sulphur.

A modification of the test consists in employing alkali instead of acid for generating the hydrogen and using a spot of mercuric chloride as in the customary test for arsenic in glycerin.

U.S. fixed limit of impurity for arsenic and heavy metals at 1 in 100,000, and employs this test modified for the former.

**Modified Apparatus for Gutzeit's Test.**—Four ounce wide mouth bottle, fitted with I.R. cork and glass tube 200 mm. long and internal diameter 5 mm., open at both ends, the lower end drawn out with small hole about 1 Cm. from end at constriction. This arrangement allows condensed water to drip back into bottle while providing free upward passage for the gas. Roll of lead paper 10 Cm. long prepared with 10% solution of lead acetate and subsequently dried and pushed into tube so that upper end is 2 cm. from top of tube. Cap of mercuric chloride soaked filter paper (5.5 cm. in diam.)



fits over top in ordinary manner. The hydrochloric acid used should contain small percentage of stannous chloride to assist in gas evolution and to reduce arsenic to the "ous" state. Also to make results comparable with the standard, which is arsenious anhydride in hydrochloric solution, strength 1 Cc. = 0.00001 Gm. Stannous chloride is made by diluting the B.P. (1898) solution with equal volume of hydrochloric acid and boiling to eliminate arsenic completely. Filter and make up to original strength. One per cent. of this is added to the strong hydrochloric acid employed in the tests. Use 10 Cc. of the acid (containing 1% stannous chloride solution), 50 Cc. water and 10 Gm. zinc.  $\frac{1}{5000}$ th milligram of arsenium calculated as arsenious oxide gives distinct yellow stain, *i.e.*, one part in 5,000,000 can be detected and estimated. In the estimation of iron compounds distil the arsenious chloride after reducing to the "ous" condition. After dissolving, *i.e.*, in hydrochloric acid and potassium chlorate, add stannous chloride drop by drop to reduce completely, as seen by the yellow colour of the solution being discharged.—C. A. Hill and J. C. Umney, C.D. ii./05,548; P.J. ii./04,500.

Method of employing arsenic free ammonium chloride and magnesium powder produces a constant stream of arsenic-free hydrogen. The compound  $\text{MgCl.OH}$  is formed. Mercuric bromide is more sensitive than mercuric chloride.—P.J. i./06,555.

**Marsh's Test** consists in generating hydrogen by means of pure acid and zinc, and to these is added the substance to be tested. If arsenic be present arseniuretted hydrogen is evolved, which deposits metallic arsenic in the cooler parts of the delivery tube, which is heated at several points by aid of Bunsen burners.

The deposit may also be allowed to form on a cool porcelain dish and is soluble in Chlorinated Lime Solution.

The addition of a little copper sulphate gave a mirror with only 0.0001 mgr. of arsenic, whereas platinic chloride (the customary addition to activate) only showed presence with 0.001 Mg.—P.J. ii./06,325.

**Reinsch's Test** consists in introducing copper to a hydrochloric solution. Cuprous chloride and hydrogen are formed. The latter reduces the arsenic to hydride; this reacts with the cuprous chloride, giving hydrochloric acid and depositing copper arsenide on the strip of metal employed.

Urine containing arsenic, methods of detection.—P.J. ii./08,402.

## ORGANIC ARSENIC COMPOUNDS.

### *Aliphatic Series.*

The following are a few of the organic arsenic bodies (aliphatic) which the author has prepared and suggests for trial. The limits of therapeutic dosage have not been determined.

① **Quinine Arrhenalate Basic**,  $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2.\text{AsO}(\text{OH})_2\text{CH}_3 = 464.212$  I. Wts. Colourless bitter crystals, melting at  $139^\circ$ , containing about 16% methyl arsenic (arrhenalic) acid, very slightly soluble in water. The corresponding strychnine salt has also been made.—C.D. ii./05,140.

② **Acidum Di-Iodomethylarsonicum.**

$\text{CHI}_2\text{AsO}(\text{OH})_2\text{H}_2\text{O} = 409.840$  I. Wts.

### *Preparation*

By oxidising with nitric acid in the cold the body  $\text{CHI}_2\text{AsI}_2$ , a constituent of the black oil formed by interaction of 5 parts amorphous arsenic with 42 parts iodoform in presence of benzene or toluene *at water bath temperature*. When the interaction is complete distil off the solvent. After oxidising, filter off the magma (much charged with iodine), wash it with cold water, and evaporate the acid liquor gently at not exceeding  $40^\circ$ – $50^\circ$ . Yellow crystals throw out containing  $1\text{H}_2\text{O}$ , which should be recrystallised from warm water.

The insoluble portion is treated with boiling benzene or toluene to remove the iodine. The residual yellow powder contains tetra-iodocacodylic acid (*v. infra*).

③ **Sodii Di-Iodo-Methyl-Arsonas**,— $\text{CHI}_2\text{AsO.OH.ONa} + \text{Aq}$ . Feathery white crystals, very soluble in water.

④ **Acidum Tetra-Iodocacodylicum**.— $\text{As}(\text{CHI}_2)_2\text{O.OH} = 641.664$  I. Wts. Small yellow crystals insoluble in water.

⑤ **Sodii Tetra-Iodocacodylas**  $(\text{CHI}_2)_2\text{AsO.ONa.6H}_2\text{O} = 771.752$  I. Wts. Beautiful yellow crystals. A very soluble compound (1 in 2). Suggested for use medicinally.

Ⓐ **Magnesii Ethylarsonas.**  $C_2H_5 AsO.OOMg. = 176.32$  I. Wts.

Prepared by treating a Potassium Arsenite Solution with Ethyl Iodide. After reaction the solution is acidified with dilute Hydrochloric Acid and filtered. Chlorine is passed into the filtrate, and Iodine removed. The liquid is made alkaline with Ammonia, treated with Magnesia Mixture in excess, and left 24 hours. The liquid is filtered and evaporated.

White powder soluble readily in acids, very slightly in water. Usually contains 1 molecule  $H_2O$ . It is decomposed by heat.

Ⓑ **Acidum Propylarsonicum.**  $C_3H_7AsO.(OH)_2 = 168.032$  I, Wts.

Prepared by interaction of Arsenious Oxide, Potassium Hydroxide and *n*-Propyl Iodide.

Ⓒ **Magnesii Propylarsonas.** Has the composition  $C_3H_7AsO.OOMg = 190.336$  I. Wts.

For these two latter bodies consult a paper by the author.—‘Organic Arsenic Compounds.’

*For further details on the aliphatic organic arsenic bodies vide Vol. I.*

### *Aromatic Series.*

**Sodii *p*-Aminophenylarsonas.** *Syn.* ARSAMIN (*c.f.* Vol. I.).

**To test the purity of Sodium Arsanilate.**

Apart from estimation of arsenic content *c.f.* Table p. 32 and determination of water of crystallisation, it may be mentioned that precipitation with Silver Nitrate is of little use to indicate arsenate as impurity. From our experiments it will not show more than 0.5% by color of the precipitate.

Sodium Arsanilate is reduced in the Marsh apparatus, yielding the usual black stain on porcelain.

**To detect Arsenate** as impurity in Sodium arsanilate we found after experimenting that the best mode of proceeding is to dissolve 0.5 Gm. in 2 Cc. Hypophosphorous Acid, warming and diluting to 10 Cc. with water, then add 5 drops Hydrochloric Acid, pass  $H_2S$  through the liquid, and warm slightly alternately. A bright orange yellow pp. will form rapidly if 0.1% Sodium Arsenate be present as impurity (W.H.M.). The Sodium Arsanilate in this method is not decomposed by the Sulphuretted Hydrogen.

Ⓓ **Acidum Dimethyl-Amino-Phenyl-Arsonicum.**  $(CH_3)_2NC_6H_4-AsO.(OH)_2 = 245.066$  I. Wts.

**Preparation—**

Dimethyl-anilin 15 Gm. are mixed with arsenious chloride 25 Gm. and heated two hours on a water-bath, and poured into 300 to 400 Cc. cold water. The mixture dissolves in the water. Add sodium hydroxide in excess until the dimethyl-anilin-arsenious oxide at first thrown out re-dissolves (it turns milky at first). Shake out the dimethyl-anilin used in excess with petroleum ether and add hydrogen peroxide to the alkaline liquor. Dilute acetic acid throws out the body.

Ⓔ **Sodii Dimethylaminophenylarsonas.** *Syn.* Sodium Dimethyl-Arsanilate.  $(CH_3)_2N.C_6H_4.AsO.OHONa.5H_2O = 357.138$  I. Wts.

Sodium dimethyl-arsanilate crystallises in leaflets, is soluble about 1 in 14 in cold water and slightly in alcohol, more so in hot and in dilute acetic and mineral acids.

Ⓕ **Acidum *p*-Tolyl-Arsonicum**  $CH_3C_6H_4.AsO.(OH)_2 = 216.032$  I. Wts. is of interest in view of a report of its efficacy on trypanosomes after recurrence with sodium arsanilate—Proc. Roy. Soc., '07, B. 79, 505.

Prepared by passing Chlorine through *p*-Tolyl-Arsenious Chloride.  $C_7H_7AsCl_2$  in presence of water, then warming to 60°–70°. The liquor is evaporated to dryness, and the substance crystallised from water.

Ⓖ **Acidum Di-Camphoryl-Arsenicum**  $(C_{10}H_{15}O)_2AsO.OH = 410.208$  I. Wts. Made by condensation of Arsenious Chloride with Sodium Camphor in dry Toluene, hardly soluble in water, readily in Benzene, Chloroform, etc. The alkali salts are, however, extremely soluble.

### ESTIMATION OF ARSENIC IN ORGANIC SUBSTANCES.

Several methods are provided in a paper by the author on ‘Organic Arsenic Compounds.’ Int., Cong., 1909. The following is simplest (arranged by the



Author), and gives good results : Powder the substance carefully, mixing with about equal quantity of potassium nitrate, moistening with water, then oxidise with nitric acid, taking up the dried material with acetic acid, adding sodium acetate solution, and titrating with Standard Uranium, Acetate Solution 1 C.c. = 0.0053 gram arsenium. For example 0.464 gram Arsamin required 20.2 C.c. uranium solution = 0.10706 gram arsenium = 23.08 per cent. (theory with  $4\frac{1}{2}\text{H}_2\text{O}$  = 23.4 per cent.).

P.G.V. gives the following for Sodium Arsanilate or the acetylated body :— 0.2 Gm. is placed in a 100 Cc. Jena flask with a long neck, 10 Cc. of sulphuric acid and 1 Cc. of fuming nitric acid are added, and the mixture boiled for one hour. On cooling, 50 Cc. of water are added and then evaporated ; this procedure is carried out twice. To the cold solution 10 Cc. of water are added, and a solution of 2 Gm. of potassium iodide in 5 Cc. of water, and sufficient water to dissolve the precipitate. After standing for half an hour it is titrated (without using an indicator) with N/10 sodium thiosulphate. 1 Cc. of this corresponds to 0.003748 Gm. As.

We have not applied either of these methods to Salvarsan.

### Salvarsan.

#### Purity of Solutions.

Ehrlich laid stress on the fact that solutions of the compound must be prepared with FRESH DISTILLED WATER. Serious after effects are stated to have been produced by, or at any rate to have some connection with, distilled water bacterially contaminated. His theory is that the cells of the patient's body become extra susceptible to the action of arsenic under the influence of the dead bacterial bodies, with the result that the "therapia sterilisans" process proceeds unsatisfactorily. It is to be noted that this expression emphasises the importance of not only germ-free water, but also water free from dead bacteria. Water absolutely above suspicion can be produced by rejecting the first distillate—indeed the steam should be allowed to thoroughly blow through the condenser, while the cooling water is cut off before commencing distilling. Every precaution must be taken to keep dust from receivers, etc. After filling stock bottles the same must then be sterilised by heat. This water will then fulfil Ehrlich's requirements.

In preparing injections, all vessels employed should be sterilised by heating at 150° C. in a hot-air chamber or in steam. The saline solution must be above suspicion and germ-free. The mortar must be covered with a large funnel to prevent access of the bacteria falling in the room. The lip of each bottle used, whether it be water or sodium hydrate or saline, should be "burnt off" in bacteriological style. The "Apotheker Zeitung" (No. 89, 1911, p. 931) points out that even with these precautions the pharmacist has no guarantee either that the Salvarsan tube is free from air organisms or that Salvarsan has bactericidal action on air organisms. The pharmacist cannot dispense a germ-free injection of a substance that will not stand boiling. All that can be done is to take all possible and reasonable precautions to exclude excess of bacteria.—C.D. ii./11,787.

*c.f., also Aqua Destillata, p. 254.*

**Tests.**—1 in 10 solution should be clear and be neutral to Congo Red paper. If 5 Cc. of Solution (1 in 10) be precipitated with 4 Cc. of Sodium Acetate Solution by warming for a short period on the water-bath and then filtered, the filtrate acidified with Hydrochloric Acid, should not be affected by  $\text{H}_2\text{S}$ . Another portion of the filtrate mixed with 3 Cc. of Ammonia and 3 Cc. of Magnesia Mixture should not deposit or become turbid after long standing.

Ferric Chloride gives a deep blood-red colour not discharged by Concentrated Hydrochloric Acid. Further tests for identity *v. P.J. ii./11,383.*

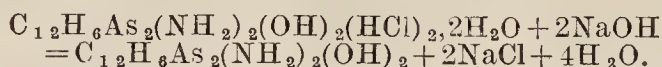
We found that a 1% solution in an amber bottle decomposed in about 48 hours giving a deposit which re-dissolved in acid or alkali but gave no reaction for inorganic Arsenic. The supernatant liquor turns dark. There was no apparent change in 24 hours in the same sample, but in white glass test tubes there were signs of decomposition in less than 24 hours.

#### Chemistry of the Injections.

The reaction which takes place on bringing sodium hydrate sufficient



to neutralise in contact with dioxy-diamino-arsenobenzo-hydrochloride may be indicated thus:



i.e. approximately :—

475.004 Gm.	requires	2000 Cc.,	N/1 NaOH	= 455.84 Cc.	15% w/w NaOH		
0.1	„	„	0.42	„	„	= 0.09	„ „ „ or $1\frac{1}{2}$
0.2	„	„	0.84	„	„	= 0.19	„ „ „ 3
0.3	„	„	1.26	„	„	= 0.28	„ „ „ $4\frac{1}{2}$
0.4	„	„	1.68	„	„	= 0.38	„ „ „ 6
0.5	„	„	2.10	„	„	= 0.48	„ „ „ 8
0.6	„	„	2.53	„	„	= 0.57	„ „ „ 9
0.7	„	„	2.95	„	„	= 0.67	„ „ „ 11

minims.

We see from the above that the **basic substance** is formed and is precipitated from solution.

This is the **Neutral 'Suspension'** as used in the *intramuscular injection*. Using *double* the amount of alkali in each case will produce the soluble Disodium Compound  $\text{C}_{12}\text{H}_6\text{As}_2(\text{NH}_2)_2(\text{ONa})_2$  as employed *intravenously*. Clearly before the basic body is produced, by the use of half the amount of Sodium Hydrate in the above formula the Monohydrochloride



By the use of  $1\frac{1}{2}$  times the amount of Sodium Hydrate in the directions for making the neutral suspension the Mono-Sodium Compound  $\text{C}_{12}\text{H}_6\text{As}_2(\text{NH}_2)_2(\text{ONa})\text{OH}$  is produced as an intermediary stage.

#### Reaction of Solutions used in Injection and attendant pain.

We have always attributed some at least of the untoward results from the substance and the pain produced to faulty technique.

Undue acidity or alkalinity would naturally tend to produce pain and inflammation. Faintly acid injections are neutralised by the blood plasma which is met in the tissues.—B.M.J.E. i./11, 15, 16.—C.f. notes under Intravenous Injection.

In our book 'Salvarsan' we give a critical survey of the reaction of all the various solutions advised by the early workers—some were markedly alkaline.

#### Untoward Results—Arsenic Retention—Deaths.

Arsenic retention is likely to occur by the intragluteal method of injection hence the intravenous method has been more advised.

36 days after an intramuscular injection a very large proportion of the Arsenic may be still found in the muscles. Inflammation may hence occur.

**Deaths.**—A case of death after 0.5 Gm is reported. The case in question was the subject of much complication, bad nutrition and respiration, hypoplasia of the heart.—Münch. Med. Woch., No. 35 Aug. 30, 1910 p 1822

Ehrlich says death may be a matter of idiosyncrasy.

A death is reported with 0.5 Gm. injected in the scapular region without and local reaction. Patient had had two apoplectic attacks. Poisonous symptoms developed in nervous system. Tremor, sweating, loss of strength—no symptoms in the digestive organs. Temperature rose to  $39.8^\circ\text{C}$ ., died on the fifth day with appearance of advanced heart paralysis. Post-mortem examination showed acute parenchymatous degeneration of the organs. Münch. Med. Woch., No. 42, Oct. 18, 1910, p. 2183.

Death of a child ten days old after 0.02 Gm.—Münch. Med. Woch., No. 42, Oct. 18, 1910, p. 2214.

Two cases of necrosis of the gluteal muscles after injection have been recorded. In one case death occurred ten days after the injection, in the other six weeks.

A death (a case of supposed cerebro-spinal syphilis) was hastened by a dose of the substance. Important to conduct a "Wassermann" before injecting with Salvarsan.—Salvarsan by M. and W., p. 44.

EHRLICH says (Deut. Med. Woch., No. 41, Oct. 13, 1910, p. 1893). The cases of death (about 12 in 12,000 cases), refer almost exclusively to cases of severe affections of the nervous system, tabes complicated with cystitis and cachexia, bulbar manifestation, patients with extensive epidermal softening and the like.

**Death following.** Three hours after intravenous injection vomiting, diarrhoea and sweats supervened, ultimately delirium, great cold, bowels unmoved, raging thirst, coma and death. Anuria said to be the cause. The author says

dose must *always* be in *emulsion and intramuscular*, as thus it is more slowly absorbed.—B.M.J.E. i./11,71. Reported by E. L. Morata—Revista de Medicina y de cirugía Practicas, Feb. 28, 1911.

Death at German Hospital, London. Patient suffered from locomotor ataxy. Subcutaneous injection.—W. W. W. held inquest on this case.

Two deaths.—B.M.J.E. i./12,3.

Its use even in young and robust patients is by no means void of risk. Two American cases in which acute nephritis was produced by 0.6 Gm intravenously in one case fatal anuria followed L. ii./11,1085. A robust man of 35 received 0.3 Gm. for a relapsing palmar and plantar syphilide intravenously. On the sixth day a further injection of 0.4 Gm. Congestion of the face, vomiting and epileptiform convulsions followed and died comatose.—L. ii./11,1286. A physician of 40 contracted a chancre on the septum nasi. Received two doses of 0.4 Gm., also as prophylactic a course of Mercurial tabloids. Death.—Details of the necropsy are given—reported by Prof. B. Fischer. A case of fatal jaundice following is also reported. An early case of general paralysis received 0.5 Gm. in Ireland with fatal result.—B.M.J. ii./11,1473, L. ii./11,1556. Most of the cases of death have followed a second injection. Prof. Fischer suggests that anaphylaxis may play a part. Ehrlich's (latest lecture.)—L. ii./11,1786.

Ehrlich on the proportion of deaths.—In view of the fact that more than 100,000 injections have been given, the proportion of accidents is comparatively small.—One of Ehrlich's recent lectures.—L. ii./11,1303.

"X" Rays and Arsenobenzol injections.—K. Ullmann and M. Haudek (Wien. Klein. Woch., No. 3, 1911) have shown by "X" rays that with the acid emulsion (Salvarsan as such in Oil or Liquid Paraffin?) the deposit of Arsenic persisted in the tissues almost without exception for a time which varied from several weeks to several months, the time being much longer than for the Mercurial preparations. The authors conclude that single injections of large doses are not to be recommended.—B.M.J.E. i./11,91.

Urine retention which lasted some days has been noticed; albuminuria also seen as an effect of the injection; disappearance of patellar reflexes; marked tenesmus and constipation. These symptoms thought to be very similar to those which accompanied Atoxyl.

The cessation of Arsenic output in the urine does not necessarily mean that there is no more Arsenic in the body; on the contrary, there may be a considerable deposit of Arsenic in the muscles which may lead to poisoning, especially if the dose be repeated.

Necrosis observed at the site of injection.—B.M.J. i./11,792.

The sloughs resulting on intramuscular injection on analysis, including those which formed three or four months after the injection, were found to contain large quantities of Arsenic, thus after a dose of 0.4 Gm. an amount of Arsenic = to 0.075 Gm. of Salvarsan was found in one slough four months later.—L. i./11,726.

The excretion period of the Arsenic is shorter after subcutaneous than after intramuscular injection. Simultaneous application of Mercury delays the excretion, whilst application of iodides shortens its duration.—B.M.J. ii./10,1274.

Arsenic found in the urine 30 minutes after injection of 0.6 Gm. intravenously.—Stopford Taylor.—L. i./11,1413.

Ehrlich (Münch. Med. Woch., No. 1, 1911), also "Experimentelle Chemotherapie der Spirillosen" states that quite contrary to any evil results on the eye being expected, eye affections (iritis gummosa and optic neuritis) have been wonderfully treated.

**A Bibliography of Deaths** from Salvarsan concluding a paper by Sir Malcolm Morris.—L. ii./13,1243.

Two deaths from intravenous use.—Hirsch, B.M.J.E. i./13,24.

Histological changes in Salvarsan poisoning.—Why Salvarsan may be given with impunity so frequently and yet an ordinary dose prove fatal as in the case reported remains a problem.—L. ii./12,1234.

About 200 cases of deaths and of cases of blindness, deafness, encephalitis, hæmorrhagica, paralysis, epileptiform convulsions and grave poisoning after Salvarsan have been recorded. It is stated that many cases are concealed.—Dr. Med. Drew, L. ii./13,1290.

Neosalvarsan given to mice in small doses was found to increase the vitality of tumours and to stimulate metastasis. Quinine Bisulphate, however,



had a pronounced retarding effect. Opium extract had no influence one way or the other.—T. Mironescue, *Comptes Rend*, 1914, 158,893; P.J. i./14,772.

Salvarsan is sufficiently safe to be used for routine treatment of syphilis in the Army. Gibbard and Harrison, R.A.M.C., Jl., March, 1914, per M.P.C. i./14,451.

**Estimation of the Arsenic** excreted in the urine has been conducted, the general *Conclusions* being (a) the elimination begins rapidly; (b) the duration of the passing of Arsenic in the urine is longer than was thought; (c) after *subcutaneous* injection the elimination is concluded more rapidly than in the intramuscular method; (d) simultaneous use of Mercury caused delay in eliminating the Arsenic; (e) Potassium Iodide given at same time shortens the duration of the Arsenic elimination.

It appears the excretion is much slower with Salvarsan than with Atoxyl or Arsacetin when injected subcutaneously; also that whilst Atoxyl and Arsacetin are excreted quickly and almost completely by the urine in the case of "606" the Arsenic is largely to be found in the fæces.

After hypodermic, gastric or intramuscular use the elimination of Arsenic in the urine lasts about 25 days. The Arsenic, it is said, is largely changed into the ionic condition, and this may be related to its antisyphilitic action.—J.C.S.A. ii./12,968.

### Recognition in Medico-Legal Cases.

The behaviour of Salvarsan with the usual reagents for Arsenic investigated to find a method of distinguishing between it and inorganic arsenic in medico-legal cases.

Muscle from a patient who had died three weeks after injections of Salvarsan still gave reactions for Arsenic. Arsenic can be recovered from Salvarsan by decomposing the latter with HCl. & KClO<sub>3</sub>. The drug gives the Reinsch, Marsh, Gutzeit, and biological tests for Arsenic. The following serve to distinguish Salvarsan from inorganic forms of arsenic. With Bettendorf's reagent it gives an amorphous, yellow ppt. which dissolves on warming and reappears on cooling. H<sub>2</sub>S gives no ppt. even after a solution of the drug has been boiled c. HCl. The organic part of the Salvarsan molecule gives certain reactions, which may afford confirmatory evidence of the presence of the drug, thus:—the corresponding diazo-derivative gives a characteristic red to violet precipitate with  $\alpha$ -naphthylamine, which may be isolated and examined for arsenic by the Reinsch or Gutzeit test. Atoxyl behaves similarly, giving a red azo-dye, but the diazotised Salvarsan gives no colour with  $\beta$ -naphthylamine, whilst Atoxyl gives a vermilion-red azo-colouring matter with the  $\beta$ -amine. Minced horseflesh sprayed with Salvarsan solution and kept for 14 days was extracted with Alcohol, slightly acidified with HCl. The residue so obtained gave positive results with the Reinsch, Gutzeit, and  $\alpha$ -naphthylamine tests, but negative results with Bettendorf's reagent, and with hydrogen sulphide. So far it has proved impossible to obtain good results by applying to Salvarsan ordinary toxicological methods for the estimation of arsenic, the latter being obtained only to the extent of from 29 to 29.5% out of the 34% present.—J.C.S.A. ii./11 448.

### Wassermann's Reaction, Effect on.

Results with regard to Wassermann's Test, subsequent to injection vary. One authority states four out of 27 primary cases were negative to the test after injection, whilst in the case of 23 paralytic cases giving + reaction, a comparatively small proportion gave negative subsequently. In a larger proportion there was reduction in extent of response to the test.

Neisser "was struck by the fact that only 10% of the cases treated showed a transition from a + to - Wassermann, while recurrences were also observed in some cases."

Another operator says 50 out of 52 cases lost their positive reaction to the test in fifty days. It is believed that the arsenical body has no action on the test. Experimentally it was found to neither hinder nor favour hæmolysis. It is well known to be otherwise in the case of Mercury.

In one case, Wassermann's test changed to negative in 40 hours.

Ehrlich states that a + reaction occurring after—subsequent to injection is analogous with recurrence without external symptoms, and hence is an indication to inject again. It will be of great value to conduct the reaction systematically from time to time on cases which have been treated with Salvarsan so as to ascertain whether an actual cure has been established.



The reaction, according to another, cannot give conclusive result with regard to success of the injection until after six or eight weeks.

*Congenital* syphilis tends to give + Wassermann throughout life and this is not altered, however much Mercury is given. *That* positive reaction should not be taken as indication that Salvarsan has no effect on the Wassermann's reaction in congenital syphilis. In *late acquired* syphilis on the other hand Salvarsan may change the reaction.—McDonagh.—L. ii./10,1490.

If at the end of the third week after injection the patient does not give negative reaction, advisability of giving a second dose is to be considered.—L. i./11,14,16.

Vagaries of Wassermann's Reaction before and after treatment.—H. C. French.—L. ii./12,228.

**Salvarsan as a Test for Syphilis.**—There is evidence that a spirochæte infection that has been in abeyance can be roused into sufficient activity to cause the Wassermann reaction to become positive, where previously (before injection) it had been negative. This result will enable the injection to be used as a test to say whether or not patient is cured of syphilis.—D'Arcy Power, B.M.J. ii./12,1606.

**Blood Examination.**—Blood examinations show leucocytosis after injection in some cases. May be as high as 30,000. Usual count is about 17,000 (McDonagh). See also Pernicious Anæmia, Vol. I., p. 175.

**Examination for Spirochetes.**—The spirochetes are stated to disappear from the blood in about 24 to 48 hours after injection, but it may take considerably longer, *e.g.*, up to 14 days.

An experimental comparison (using rabbits) between "606," Mercuric Iodide and Potassium Iodide as antisypilitics: Salvarsan was the most marked spirochæticide, Potassium Iodide found to be not a direct antisypilitic.—L. ii./11,940.

**What happens to the Spirochetes?**—Ehrlich has stated that Salvarsan kills the spirochetes and the dead spirochetes liberate a protein which stimulates the production of a syphilitic antibody, and that on the extent to which this is effected the cure of syphilis depends.

McDonagh says parasitotropic substances act partly by killing the parasite and partly by liberating the chemical substances contained in the bodies of the parasites which kill off the remainder. That Salvarsan acts in this way is shown by the fact that larger doses are required to heal an early case with a primary sore, than a late case with gummata. Again, the cure of infants from infected mothers by injection of the latter (no Arsenic passing by the milk) is also in support of this view.—B.M.J. ii./10,1261.

Another authority says that the spirochetes become broken up into bead-like bodies or pieces by the action of the chemical—this at any rate in vitro. The spirochetes can be found in teeming numbers in a chancre before the injection, whilst the day after the injection they will have disappeared.

A pharmacologist writes:—"The parasites in the case of Salvarsan and Sodium Arsanilate, are able to break up the molecule and so liberate the arsenic in ionic form—such ionic arsenic is very toxic to protozoa. Suggestion is made that an Organic Mercury Compound might also work well on bacteria on analogous lines.—P.J. ii./11,16.

Another opinion is that it is too premature to say whether the effect consists in destruction of the whole or part of the parasites or simply in suppression of their activity.—L. i./11,731.

The spirochætes are *actually destroyed* by the intravenous injection.—D'Arcy Power, B.M.J. ii./12,1606.

Table of some Organic Arsenic Compounds shewing Molecular Weights, Content of Arsenium, (As), and Solubilities.

ARSENIC COMPOUND AND FORMULA.	Molecular Wts., employing Inter- national 1915 Atomic Wts.	Arsenium content per cent.	SOLUBILITIES.	
			Water.	Alcohol 90%
Acid, Arsenic, $\text{AsO}(\text{OH})_3$ . ... ..	141.984	52.8	2 in 1	Very
Acid, Cacodylic, $(\text{CH}_3)_2 \text{AsO.OH}$ . ... ..	138.016	54.3	2 in 1	1 in 4
Cacodyle, $(\text{CH}_3)_2 \text{As} - \text{As}(\text{CH}_3)_2$ . ... ..	210.016	71.4		
Cacodyle Oxide $(\text{CH}_3)_4 \text{As}_2\text{O}$ . ... ..	226.016	66.3		
Calcium Cacodylate $[(\text{CH}_3)_2 \text{AsO}_2]_2 \text{Ca}$ ... ..	314.086	47.7	2 in 1	1 in 2
Sodium Cacodylate $[(\text{CH}_3)_2 \text{AsO.ONa}3\text{H}_2\text{O}$ . ... ..	214.056	35.0	2 in 1	About 1 in 1
Magnesium Cacodylate $[(\text{CH}_3)_2 \text{AsO}_2]_2 \text{Mg}$ . ... ..	298.336	50.25	1 in 3	Insoluble
Iron Cacodylate $[(\text{CH}_3)_2 \text{AsO}_2]_3 \text{Fe}$ . ... ..	466.864	48.17	1 in 15	Insoluble
Guaiacol Cacodylate, $(\text{CH}_3)_2 \text{AsO.OH.C}_6\text{H}_4.\text{OH}(\text{OCH}_3)$ . ... ..	262.080	28.6	1 in 25	1 in 1.5
Strychnine Cacodylate $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2(\text{CH}_3)_2$ $\text{AsO.OH}$ ... ..	472.212	15.8	hardly	1 in 80
Acid, Ethyl-cacodylic (diethyl-arsinic), $(\text{C}_2\text{H}_5)_2 \text{AsO.OH}$ . ... ..	166.048	45.1		
Acid, propyl Cacodylic, $(\text{C}_3\text{H}_7)_2 \text{AsO.OH}$ . ... ..	194.080	38.6		
Di-sodium Methylarsenate (Arrhenal) $\text{CH}_3\text{AsO}(\text{ONa})_25\text{H}_2\text{O}$ . ... ..	274.064	27.3	1 in 1	Slightly
Quinine Arrhenalate, $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2\text{CH}_3\text{AsO}$ . $(\text{OH})_2$ ... ..	464.212	16.1		
Acid, Di-iodo Methylarsonic $\text{CHI}_2\text{AsO}(\text{OH})_2\text{H}_2\text{O}$ ... ..	409.840	18.2	1 in 10	1 in 10
Sodium Di-iodo Methylarsonate $\text{CHI}_2\text{AsO}(\text{OH}).\text{ONaAq}$ . (on anhydrous salt) ... ..	413.816	18.1	1 in 1	Slightly
Acid, Tetra-iodo Cacodylic $(\text{CHI}_2)_2 \text{AsO.OH}$ . Sodium Tetra-iodo-Cacodylate $(\text{CHI}_2)_2 \text{AsO.ONa.6H}_2\text{O}$ . ... ..	641.664	11.7	Insoluble	1 in 600
Magnesium Ethyl Arsonate, $\text{MgAsO C}_2\text{H}_5\text{O}_2$ $(\text{OH})_2$ ... ..	176.32	42.5	1 in 2 Very slightly	Slightly Almost insoluble
<i>n</i> -Propyl-arsonic Acid. $\text{C}_3\text{H}_7\text{AsO}(\text{OH})_2$ . ... ..	168.032	44.6		
Magnesium Propyl Arsonate $\text{C}_3\text{H}_7\text{AsO.O}_2\text{Mg}$ . ... ..	190.336	39.4	Pract. insoluble	
<i>p</i> -Tolyl-Arsonic Acid $\text{CH}_3\text{C}_6\text{H}_4\text{AsO}(\text{OH})_2$ ... ..	216.032	34.7	Slightly (more so hot).	Slightly
<i>p</i> -Amino-phenyl-Arsonic Acid. $\text{NH}_2\text{C}_6\text{H}_4\text{AsO}(\text{OH})_2$ (Arsanilic Acid) ... ..	217.034	34.5	Slightly	Slightly
Sodium <i>p</i> -amino-phenyl Arsonate $\text{NH}_2\text{C}_6\text{H}_4.\text{AsO.OH.ONa.}+4\text{H}_2\text{O}$ . ... ..	311.090	24.09	1 in 6	1 in 125
Ditto Ditto Anhydrous. Mercury Atoxylate. $(\text{NH}_2\text{C}_6\text{H}_4\text{AsO.OH.O})_2\text{Hg}$ . ... ..	239.026	31.4		
Sodium Acetyl- <i>p</i> -Amino-Phenyl- Arsonate. $\text{CH}_3\text{CO.NH.C}_6\text{H}_4\text{AsO.OH.ONa.5H}_2\text{O}$ ... ..	632.652	23.7	Insoluble	
Dimethyl-amino-phenyl-arsonic Acid. $(\text{CH}_3)_2\text{N.C}_6\text{H}_4\text{AsO}(\text{OH})_2$ ... ..	371.122	20.2	1 in 10	Insoluble
Sodium Dimethyl-Amino-Phenyl- Arsonate. $\text{CH}_3)_2\text{N.C}_6\text{H}_4\text{AsO.OH.ONa.5H}_2\text{O}$ . ... ..	245.066	30.6	Almost insoluble	Almost insoluble
	357.138	21.0	1 in 14 (more in hot).	Slightly (more if hot).



ARSENIC COMPOUND AND FORMULA.	Molecular Wts. employing Inter- national 1915 Atomic Wts.	Arsenium content per cent.	SOLUBILITIES.	
			Water.	Alcohol 90%.
<b>Acid Di-camphoryl-arsinic.</b> (C <sub>10</sub> H <sub>15</sub> O) <sub>2</sub> AsO.OH. ... ..	410.208	18.3	Hardly. 1 in 5	Easily. 1 in 12
<b>Dioxy-diamino-arsenobenzol Di- hydrochloride</b> C <sub>12</sub> H <sub>12</sub> O <sub>2</sub> N <sub>2</sub> As <sub>2</sub> (HCl) <sub>2</sub> .2H <sub>2</sub> O	475.004	31.56		
<b>Neosalvarsan</b> C <sub>13</sub> H <sub>13</sub> O <sub>4</sub> N <sub>2</sub> SAs <sub>2</sub> Na ... ..	466.114	32.1	Readily. Very soluble.	Very Slightly. Very soluble.
<b>Sodium Benzo-sulpho-<i>p</i>-amino-phenyl Arsonate</b> C <sub>6</sub> H <sub>5</sub> .SO <sub>2</sub> .NH.C <sub>6</sub> H <sub>4</sub> .As.O.OH.ONa. ...	379.128	19.77		

Prof. A. D. Waller, of the Physiological Laboratory, London University examined several of the soluble substances which the writer prepared. On the Sartorius muscle of frog it was found, for example, that a 5 per cent. solution of di-iodo-methyl-arsonic acid, CHI<sub>2</sub>AsO(OH)<sub>2</sub> was infinitely more active than a solution of dimethyl-arsamin of the same strength. Indeed, the latter substance was comparatively non-toxic. Neither of these substances have been employed in medicine. It should be noted that both substances contain practically the same content of arsenic—namely, 20 per cent. approximately. They are, however, very different in chemical constitution. In addition the following in solution were compared:—

Sodium tetra-iodo-cacodylate.  
Arsamin.  
Arsacetin.  
Sodium di-iodo-methyl-arsonate.

Arsamin and sodium di-iodo-methyl-arsonate had apparently the least effect on muscle, whilst of this series arsacetin had more, and sodium tetra-iodo-cacodylate was the most potent. From these results there would seem to be some utility for the *sodium-di-iodo-methyl-arsonate* by reason of its relative non-toxicity, combined with its high content of iodine in addition to arsenic.

Similarly the *Sodium tetra-iodo-cacodylate* compound should be worthy of trial—but this is more toxic.

With regard to the non-toxic bodies, *sodium dimethyl-*p*-amino-phenyl-arsonate* seems worthy of attention, as also does *p*-tolyl-arsonic acid, which was found, as mentioned earlier, to be active on trypanosomes.

The muscle test is only applicable to soluble substances.

G. T. Morgan determined the carbolic acid coefficient of a number of these substances; the coefficient of the di-iodo-methyl arsonic acid to *B. coli communis* is very high—much higher than that of sodium arsanilate.

Attention may here again be drawn to *p*-**Amino-phenyl-arsonic Toluene Sulphonate** (Vol. I., p. 190), which has recently been investigated.

## AURANTIUM.

**Terpeneless Oil of Orange** (*c.f.*, also Table of Essential Oils, p. 100).

A note from Sicily says the process of manufacture is exactly similar to that for terpeneless Lemon Oil, *q.v.*, except that a larger quantity of Terpenes are distilled off—about 95%. No physical or chemical data are known for the finished product, as it is only very rarely distilled, and then it is not a great success. The odour of the Terpeneless Orange Oil does not pay for the distillation in many cases.—The Terpeneless Orange Oils on the market are



usually "synthetic" products, *i.e.*, a mixture of which the chief odoriferous constituent is Methyl methylantranilate. The distillation in London and elsewhere is carried out more scientifically than in Southern Italy.

**Neroli Oil (Artificial)** is a mixture the chief body of which is the methyl ester of Anthranilic Acid.—P.J.ii./o6,377—to this the fragrance of the natural oil is due.

*For genuine Neroli Oil, see Vol. I.*

Concerning all the varieties of the genus *Citrus* and uses of.—P.J. ii./o6 717. *See also* Allen, 4th Edn., Vol. IV., p. 359.

**Petitgrain.**—This name is given to the young orange fruits which fall naturally after "setting." Oil of Petitgrain is distilled from them.

**Petitgrain Oil.**—Adulteration with Terpinyl Acetate. Detection by taking saponification value at 1 and 2 hours.—P.R., 1912,3,240.

Paraguay produces Oil of Petitgrain.—P.R., Dec., 1913, p. 414.

## BELLADONNA.

### Assay and Alkaloidal Content.

Methods of assay of leaves, root, and extract.—P.J. ii./oo,195 ; i./o3, 268 *vide also* C.D. ii./o6,839.

Farr and Wright found a minimum of 0.14 and a maximum of 1.32% (exceptional) total alkaloids in the leaves; an average of 0.547%—rather more than is generally found in the root.—P.J. i./o5,398 ; C.D. i./o5,425.

Roots of our own growing gave the following:—Second year's growth, 0.605% ; fourth year's, 0.51%. Three years is believed to give about the best yield.

Cæsar and Loretz's method of assay is described.—C.D. i./o8,21.

MacEwan and Forrester supplied figures indicating variability of the alkaloidal content—0.10 to 0.65%—the most frequent value being 0.451, and the mean 0.339%. Galenical preparations of Belladonna differ in action from the alkaloids contained. Alkaloid determination does not suffice. Thoms, it may be recalled, found in two Belladonna Extracts (P.G. earlier edition) each containing 1.72% alkaloids, 3.5 and 8.1% Tannin, 1.8% of other organic bases (in each); Permanganate numbers 81 and 256; and 15.7 and 11.5% volatile matter,—showing that alkaloidal determination is not finality in evaluation. There is much divergence regarding pharmacopœial requirements, and analyses are necessary with the view of ascertaining if the drug is harvested at the proper season.

**Cultivation** of Belladonna in America.—Two crops of leaves are obtained—one at end of July and the second in October. If the roots are not required for use they should be taken up in October and buried in a shed to preserve from frost, to be divided into five or six rootlets in the spring for propagation. This procedure is better than growing from seed. An acre yields six to eight thousand pounds of herb.—Am. Jl. Ph., 1909,811 ; P.J. i./o9,150.

The highest alkaloidal content was obtained from a plot which had not been manured at all, but which was **fully exposed to the sun**. This content (1.035% in the dry leaf) from leaf collected September, 1911, was the highest ever recorded as having been obtained. The content from leaves under similar conditions, September, 1910, was 0.44%, June, 1911, 0.65%,—each the highest as against plants grown with artificial manures and far in excess of the yields from plants grown *in the shade*.—F. Ransom and H. J. Henderson, Int. Cong. Applied Chemistry, 1912. This is of especial interest more particularly as Belladonna and Digitalis are frequently found in nature in partially shaded situations. Indeed, it has been advised to grow Belladonna in the shade. The results also are exactly analogous with the author's cultivation of Digitalis. He has found (*c.f.*, "Digitalis Assay") that plant grown in the sun were the most active both by chemical and physiological assay.

**Artificial Manures.** *e.g.*, Sodium Nitrate 1 cwt. with Kainit 3 cwt. per acre, increase the yield of *green plant* per acre. This yielded 13½ tons per acre September, 1911, as against the plot with no manure, but sun, 8½ tons per acre.—Ransom and Henderson, *ibid*.

Belladonna leaves grown in the shade contained 0.35% total alkaloids,—that grown in the sun 0.4%.—W. Unger, Y.B.P. 1913,261.

Basic Slag 2 cwt. per acre and Superphosphate (5 cwt.) applied March to April had good effect on alkaloid yield,—better than farmyard manure.

The highest percentage of alkaloids has been observed in sunny seasons. Cultivated plants yielded as much as 1.08% alkaloid.—F. H. Carr Int. Congress App. Chem., C.D. 1912, p. 432; Y.B.P. 1913.

Experiments by A. F. Sievers at the Office of Drug Plant Investigation, Washington, on *Atropa Belladonna* (first, second and third year's growths) showed that the alkaloidal content of the leaves of first year's plants (1910) gave an average of 0.547%, the highest being 0.7% and the lowest 0.334%; the same plants yielding approximately the same amount of alkaloid from season to season. The leaves can be picked to best advantage from the time of flowering until the early berries begin to ripen. Later the leaves are richer, but are too small and sparse for harvesting.—C.D. i./14,52.

*Epitrix Atropæ* Foudras. A small beetle has made its appearance in *Belladonna* plants at Hitchin, especially prevalent in dry seasons. Recommendations are given for cultivation which would tend to eradicate the insect.—Perrédès, P.J. ii./10,135.

*Belladonna* Fruit, either ripe or unripe, contains 0.1 to 0.13% Alkaloids.—P.J. ii./09,473.

Frogs' and rabbits' livers have the power of destroying Atropine. This is due to a soluble body resembling a ferment. None of the tissues investigated in the cat, rat and dog have any like power.—B.M.J. ii./12,1099.

Elimination of a *Belladonna* preparation taken internally is rapid. It rarely produces poisonous effects.—L. ii./10,575.

### **Extractum Belladonnæ Viride (B.P. 1898).**

Microscopical identification of constituents.—P.J. ii./08,834.

Extracts prepared from the dried drugs have replaced the green extracts in the Continental Pharmacopœias, agreeing with the F. I. requirements. Experiments using various parts of the plant, fresh leaf, subaerial stem, etc., and extracting by various methods showed that the fresh herb dried and percolated to exhaustion with 70% alcohol, the alcohol distilled off the precipitated resin and chlorophyll filtered off and the filtrate evaporated gave an extract with alkaloid content of 2.2%,—much higher than any of the others.—P.J. ii./11,35.

A sample yielded 1.03 and 1.18%. A foreign Extract yielded 0.42%.—Had been reduced by adding an inert extract.—Southall Rep. 1913, p. 42.

### **Extractum Belladonnæ Alcoholicum (B.P. 1898).**

In the 1898 official process of assay, the fatty matter should be first removed by shaking the sample (acidified) with chloroform.—P.J. i./99,432. Modes of assay.—P.J. i./03,268.

Ether preferred to chloroform as the immiscible solvent, and a little tragacanth may be added to assist separation.—P.J. ii./00,195; Y.B.P. 1901,40.

### **Extractum Belladonnæ Foliorum (Alcoholicum).**

The average yield was found by Farr and Wright to be 1%. The stronger the alcohol used the better the extraction—using 90% alcohol, 4% alkaloids were obtained against 2.15% only when employing 50% alcohol.

For POWDERED EXTRACT, powdered leaves recommended as diluent; should be well dried first, and must contain sufficient alkaloid to permit of their being used in the proportion of 2 of diluent to 1 of extract. This keeps well.—P.J. i./05,398; C.D. i./05,425. The use of dried exhausted marc would greatly simplify.—H. Deane.

Regarding these notes, c.f., *Extractum Belladonnæ Siccum (Off.)*.

### **Fluidextractum Belladonnæ Radicis. U.S.**

More than one agitation of the chloroformic solution of the alkaloids with acid seems necessary in the U.S.P. process of estimation and two portions of water for washing the separator necessary.—Naylor, P.J. i./07,394; Am. Jl. Ph. 06,456.

## **BISMUTHUM.**

### **Liquor Bismuthi et Ammonii Citratis. (Off.).**

Sterile materials and utensils should be used. The solution of ammonia used must be quite free from tarry matter. Test for the latter by adding 2 to 3 Gm. of copper sulphate to the ammonia solution until it smells very slightly of ammonia; tar constituents will colour it.—C.D. i./05,708.



N.B.—Experiments conducted by us to determine the best method of preparing Liquor Bismuthi showed that the *B.P. 1885 method is best*,—keep the Liquor in small stoppered bottles (full) or make with Chloroform Water 1 in 400 (Chloroform is a good preservative). It is important that the Bismuth Citrate should be pure. The 1898 B.P. method was satisfactory but was, of course, a longer process. For further details of our experiments *vide* Edn. XIV., p. 184.

The *Off.* method appears open to some criticism. More water for washing than that specified may be required. And if a large amount be used there appears liability to reform some subnitrate which will not dissolve in the Ammonia. We incline to the opinion that B.P. '85 method was more economical and expeditious, especially for small quantities.

R. C. Cowley gives directions for preparing a neutral Ammonium Bismuth Citrate—a modified form of that published in P.J. and C.D. Dec. 23, 1899—Precipitated Bismuth Citrate in the freshly precipitated condition acts as a monobasic acid which can be quantitatively estimated with Ammonia Solution,—using Litmus as indicator—in this way a neutral Liquor Bismuthi can be made. It forms a clear solution with Sodium Bicarbonate (Commercial Liquor containing free Ammonia converts Bicarbonate to Carbonate,—the latter then precipitates Bismuth as Carbonate).—C.D. i./11,314; Austral. J., P. Jan. 1911.

This does not agree with practice. A considerable excess of Ammonia is always required to effect solution. Cowley's formula in "Pharmaceutical Formulas" contains  $1\frac{1}{2}$  mol. Ammonia to one of Bismuth Citrate.

Careful experiments by us showed that 1 mol. weight of commercial Bismuth Citrate required approximately 2 molecules of Ammonia to dissolve to an alkaline solution. This Solution, on adding Citric Acid to neutralise  $\frac{1}{2}$  a molecular weight of the Ammonia, becomes amphoteric to litmus. Therefore, 1 molecular weight of Citrate to make a Neutral (amphoteric) Solution requires  $1\frac{1}{2}$  molecular weights of Ammonia.

We found Sodium Bicarbonate to be compatible with this, and also with an alkaline stock liquor in the proportion of 4 grains to the drachm without causing precipitate for over a month. Precipitation, however, had occurred in the neutral solution in 3 months.

### BISMUTHI SALICYLAS.

5 Gm. treated with 50 Cc. of dry ether should yield not more than 0.005 Gm. Salicylic Acid.—*Off.*

Rectified Benzol as extractive. If allowed to percolate through the sample and the liquid be dropped into dilute Ferric Chloride Solution, this will detect the smallest quantity of free Acid by violet colouration at junction of the two liquids.—P.J. ii./08,404. Alcohol decomposes, and Ether and Chloroform are unsuitable.—P.J. i./09,3. Harrison found Ether best for extracting. A true Bismuth Salicylate and a loose combination of base and acid are on the market.—P.J. ii./09,131,156; C.D. ii./09,184.

### BISMUTHI SUBNITRAS.

**Dragendorff's Test for Alkaloids.**—Bismuth Subnitrate 8, Nitric Acid, Sp. Gr. 1.18, 20; add this solution gradually to a concentrated solution of Potassium Iodide 22.7. Cool, decant from Potassium Nitrate formed and dilute to 100 with water. The solution precipitates most alkaloids.

A suggested modification.—Dissolve Bismuth Carbonate 64 in Hydrochloric Acid 85 and add Water 500 containing Potassium Iodide 166. Finally make up with Water to 800. This eliminates Nitric Acid which causes decomposition, and the proportion of Potassium Iodide is less. With this formula there is not the trouble with the crystals of Potassium Nitrate.

**Thresh's Reagent.**—Bismuth Citrate 2.4 Gm., Water 20 Cc., Ammonia *g.s.*, made up to 30 Cc. with Water and add to a solution of Potassium Iodide 2 Gm. in Nitric Acid 45 Cc. Is similar in use to above.

### Bismuthi Tartras Solubilis.

Estimation of Bismuth content in this compound is best conducted by weighing as Bismuth Sulphide. The ash may be titrated for the Sodium Carbonate. Bismuth cannot well be determined in the ash—there appears to be some loss on ignition. Free acidity which amounts to about 12 to



15% calculated as Tartaric Acid, is arrived at by titration of the original substance with (*e.g.*, 0.5 Gm.) with N/10 NaOH.

**Metallic Bismuth** is diamagnetic. It is a bad conductor of heat. It is used in making stereo-metal on account of its low fusion point—about 300° C.—P.J.ii./13,58.

### BROMUM.

The following medicinal inorganic **Bromides** contain the halogen in these proportions:—Ammonium Bromide ( $\text{NH}_4\text{Br}$  = 97.962 I. Wts.) 81.58%, Calcium Bromide U.S. ( $\text{CaBr}_2$  = 199.91 I. Wts.) 79.95%, Lithium Bromide U.S. ( $\text{LiBr}$  = 86.86 I. Wts.) 92.01%, Potassium Bromide ( $\text{KBr}$  = 119.02 I. Wts.) 67.14%, Rubidium Bromide ( $\text{RbBr}$  = 165.37 I. Wts.) 48.3%, Sodium Bromide, (anhydrous) ( $\text{NaBr}$  = 102.92 I. Wts.) 77.6%, Strontium Bromide *Off.* ( $\text{SrBr}_2 + 6\text{H}_2\text{O}$  = 355.566 I. Wts.) 44.95% (if exsiccated about 64.59%), Zinc Bromide ( $\text{ZnBr}_2$  = 225.21 I. Wts.) 70.9%.

### ORGANIC BROMINE COMPOUNDS.

The amount of Bromine in daily doses of Organic Bromine Compounds is considerably less than the quantity in average doses of Alkaline Bromides *e.g.*, that of Potassium.

#### BROMINE IN DAILY DOSE.

Potassium Bromide	60 grains	Bromural	6.2 grains
Bromalbacid	1.8 grains	Bromalin	54 grains
Bromocoll	15 grains	Bromamide	7.38 grains
Bromipin (10%)	18 grains	Brometone	11.6 grains.

The exception is Bromalin which gives rise to toxic effects. Bromipin is clinically considered the most efficacious of these bodies. The conclusion is, therefore, that these bodies are only non-toxic owing to the small amount of Bromine they contain, or yield to the organism, and therapeutic value is limited to those cases in which such small amounts are of use. It is pointed out that the fact that the Bromine-Sesame Oil Compounds generally have not obtained any wide application in epilepsy, where the results are easily to be gauged, suggests that the Iodine analogues are equally inactive, but the cases in which they are employed do not give such definite indications of efficacy (or otherwise) of the therapeutic agent adopted.—Fortescue Brickdale, B.M.J. ii./10,1597. *c.f.* also Iodine compounds.

#### New Method of Bromination with Aqueous Hypobromous Acid.

The use of hypobromous acid, prepared by digesting bromine and  $\text{H}_2\text{O}$  with excess of  $\text{HgO}$ , in the form of a straw-yellow solution containing about 6.2% of  $\text{Br}_2$ , is suggested as a brominating agent. It suffices to shake this in the cold with  $\text{C}_6\text{H}_6$ ;  $\text{C}_6\text{H}_5\text{CH}_3$ , or  $\text{C}_6\text{H}_5\text{COOH}$  to obtain satisfactory yields of monobromobenzene, *o*- and *p*-bromotoluene, *m*-bromobenzoic acid. Aniline yields tribromaniline; phenol gives tribromophenol under similar conditions: nitrobenzene resists bromination, as also does phthalic acid.—J.C.S.A. i./10,234.

### CAFFEINA.

Caffeine and Theobromine fail to precipitate with Mayer's Reagent, distinguishing them from the majority of alkaloids. Caffeine has a bitter, not agreeable taste. Tea contains a minimum of 3.5% of Caffeine and a maximum of 4.0% (L. ii./10,143,210.) Raw coffee about 1.2% and when roasted about 1.3%. For manufacture, tea dust with the strongest yield of alkaloid is extracted.

**TEA.**—When there is neither caffeine nor tannin present in quantity exceeding that which the compound of them (caffeine tannate) contains, the tea is pronounced by the taster as of good quality. Caffeine and tannin occur mostly in good teas in the ratio of 1:3—which is virtually the ratio in Caffeine tannate.—L.i./11,46.

**TEA INFUSIONS.**—Cold water extracts only a very small proportion of the total Caffeine in Tea, though solubility is 1.35 per cent. at 16° C. Caffeine is taken up always as Tannate.—L. i./13,844.

**ESTIMATION OF CAFFEINE IN PRESENCE OF ACETANILIDE**, *e.g.*, in headache powders; extract from a sulphuric acid solution with chloroform. Precipitate with iodine and decompose the periodide with sodium sulphite, and extract the base again with chloroform.—C.D. ii./04,469.

Caffeine hinders germination of seeds.—L. i./12,666.

Determination of Caffeine in Caffeine-Sodium-Salicylate. The method of P.G.V. shaking out 5 Cc. of a 20% solution with 5 Cc. of Chloroform gives result at least 5% too low. For modification *vide* Apoth. Zeit., 1911, 26,647; P J. ii./11,437,463.

### Maté.—

Analysis showed Caffeine 2.02%, Sugar as Glucose 6.08%, Tannin 11.22%—3 and 10 minutes infusion (the 10 minutes being on the old marc) at about 90° gave total dissolved substances respectively 21.8%, 31.8%, organic matter 19.4%, 28.4%. Mineral Matter (Ash) 2.4%, 3%, Tannin 7.68%, 11.08% and Caffeine 1.39% and 1.70%. The second figures in each case indicating totals. The best method of preparing the 'Tea' is by first moistening the leaf thoroughly with boiling water, and then after a few minutes, adding the remainder of the boiling water and allowing to infuse for 15 minutes.—P.J. i./10,787.

An attempt to again introduce Maté into Europe. It would be preferable to the alcohol which threatens to destroy us.—C.D. i./11,53. A mild heart stimulant if taken periodically. Leaving it off after having taken it for some time may cause prostration.—P.J. i./11,3. Mortality from heart disease in Argentine is greater than elsewhere—scribed to Maté. Test for distinguishing between Infusions of Tea and Maté—P.J. i./12,125.

Caffeine has been isolated from Maté leaves, but "Matteine" said not to occur in the leaves.—J. Chem. Soc., 101, II., 1086.

## CALCIUM:

**Calcium Metal** is made electrolytically.—Na. Dec. 22, 1904, p. 80.

The method consists in electrolysing fused calcium chloride with an iron cathode which only just touches the surface of the salt and can be moved outwards so as to produce ingots of the metal. Its density is 1.548, M. Pt. 810° C. Can be drawn out into a very fine wire, being tenacious. Is only slightly acted upon by water, but combines with hydrogen and with nitrogen.

For Chemical Uses, see P.J. i/05,721.

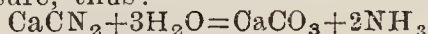
**Calcium Carbide.**  $\text{CaC}_2 = 64.07$  I. Wts.

(Requires special storing.)

Blackish crystalline masses, resembling small pieces of coal. Evolves acetylene when brought into contact with water. May be used as a test for, and in the preparation of, absolute alcohol.—P.J. i./98,139.

Carcinoma of the uterus, piece of carbide applied with success to dried ulcerated surface with a tampon over it, checks bleeding, fetor and discharge.—Münch. Med. Woch., 1900, No. 24.

When nitrogen is passed over calcium carbide heated to 1000° C. the cyanamide is also formed.  $\text{CaC}_2 + \text{N}_2 = \text{CaCN}_2 + \text{C}$ . The nitrogen of same interacts with water under pressure, thus:—



The nitrogen must first be freed from oxygen. This is effected by fractional distillation of liquid air. **Calcium Cyanamide**,  $\text{CaCN}_2 = 80.09$  I. Wts. formed can be utilised as manure and for other purposes.

The above method of fixing atmospheric nitrogen is the **Frank-Caro** process.

Another—the production of Calcium Nitrate is that of **Birkeland-Eyde**. A third is the production of nitrous fumes by passing air through an iron tube in which an alternating current arc of 5 metre length is maintained under a pressure of 4,200 volts.—SCHOENHERR and HESZBERGER. The gas obtained is mixed with limestone, forming Calcium Nitrate, the 'Air Saltpetre.'—Na., Nov. 25/09, p. 114.

## CALCII CHLORIDUM.

There is a possible danger of Calcium Chloride administered in excess causing clotting of the blood. Sir J. Barr refers to Blair Bell's Calcimeter, *i.e.*, an Apparatus for estimating the proportion of Lime Salts in the blood, urine and other fluids. Such estimation may show lime in excess, and suggest the use of Citric Acid.—B.M.J. i./07,717.



The *method* consists in counting the Calcium Oxalate crystals formed by mixing a known volume with Oxalic Acid.

250 c.mm. of an Aqueous Solution of Oxalic Acid (1 in 30) are mixed with 100 c.mm. of blood (the necessary graduated pipette for the blood and capsule of the solution are taken to the bedside of the patient). After time has elapsed (10 minutes) for the Calcium and Magnesium to be combined, 250 c.mm. of a mixture composed of Acetic Acid (1%) 95 parts and Glycerin 5 parts are added—this dissolves Magnesium Salts. Then after a further 10 minutes add 100 c.mm. of the mixture to 500 c.mm. of Distilled water. A drop of this final dilution is counted on a Thoma Zeiss Cell. Count the number of crystals in 250 squares—1 crystal per square gives the Calcium Index 1. Normal human blood gives an average of 0.8 to 1.0 crystal per square if the specimen be taken early in the day. Great accuracy in measuring is essential.—Sir James Barr, B.M.J. ii./10,830.

Some observations seem to indicate that pregnancy is terminated when the foetus ceases to absorb or receive Calcium Salts from the mother's blood and a large accumulation occurs in her system.

**Calcium Estimation in Urine.**—The lime is thrown out by a Reagent consisting of a Saturated Solution of Oxalic Acid in 5% Solution of Acetic Acid. The volume of the precipitate is compared in a specially graduated centrifuge tube with that produced with a Standard Solution of Calcium Phosphate  $\text{Ca}_3(\text{PO}_4)_2$ —prepared by dissolving 0.05 Gm. in a little Hydrochloric Acid, making alkaline with Ammonia and then Acid with Acetic Acid. Finally 2 Gm. of Urea are added and the whole diluted to 100 Cc. Sp. Gr. of the product is about 1.015.—B.M.J. i./12,878.

In practice 5 Cc. of urine—24 hours specimen,—is rendered faintly acid with Hydrochloric Acid to dissolve any insoluble Phosphates and then made faintly alkaline with Ammonia and filtered—5 Cc. of the filtrate are placed in a special graduated centrifuge tube and 5 Cc. of Standard Calcium Phosphate Solution *as above* in another. 1 Cc. of Reagent, consisting of a saturated solution of Oxalic Acid in 5% solution of Acetic Acid, is added and 2 Cc. of Alcohol to each tube and thoroughly shaken. After centrifugalising 15 minutes the volumes of the two precipitates are compared. Then the per-

centage of Calcium in the urine is ascertained from the formula  $\frac{U}{S} \times \frac{1}{50}$  in

which U = height in millimetres of precipitate in the urine examined and S = height in millimetres of precipitate in the standard solution. If the urine contains an unusually large amount of Calcium, so that the precipitate more than fills the calibrated portion of the tube, it is to be diluted and the test repeated.

In the puerperal state the coagulation time immediately after delivery is below normal. Determination of the time might prove useful after delivery to indicate risk of thrombosis or embolism if the time be low, or of post-partum hæmorrhage if high. Treatment as above could then be employed.—L.i./08,99.

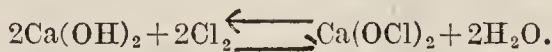
There is a connexion between thyroid secretion and Calcium metabolism also intimate connexion between pituitary extract and Calcium metabolism—under the influence of the extract there is an increase of Calcium. Adrenal Extract causes Calcium retention. The ovaries influence Calcium metabolism (osteomalacia has been cured by oophorectomy and Calcium retention occurs after the menopause). The ductless glands more than probably preserve a balance in the Calcium metabolism—one acting anabolically, another katabolically. Subsequent papers to indicate more fully the connexion existing between these glands and the functions of the female genital apparatus.—B.M.J. i./09,517.

In most cases of exophthalmic goitre (thyroid secretion in excess) the Calcium index was low, hence administration of Calcium salts may be advantageous.

Further work on the subject of menstruation gave *inter alia* the conclusion that menstruation is a periodic function only in so far as the Calcium metabolism is in harmony with this periodicity, and that the function is dependent on Calcium metabolism in all its ramifications.—B.M.J. i./09,592.

Ammonium Oxalate prevents coagulation of the blood by precipitating Calcium, the presence of which is thought to be essential to coagulation.—P.J. ii./09,657.

**Calx Chlorinata.**—According to recent views, when moist  $\text{CO}_2$  acts on bleaching powder Chlorine only is given off (no Hypochlorous Acid as originally taught). Air free from  $\text{CO}_2$  very slowly liberates Hypochlorous Acid, but no Chlorine. With air containing  $\text{CO}_2$  a mixture of Hypochlorous Acid and Chlorine is obtained, the proportion of the former decreasing with time. These points are explained on assumption that the action of Chlorine on alkalis is reversible.



The action of air in promoting bleaching is therefore due to removal of Lime from the powder by  $\text{CO}_2$ .—P.J. ii./10,584. The bleaching action is further accelerated by the addition of Common Salt or Calcium Chloride.

See Vol. I., p. 234, for **Water Sterilisation** with Chlorinated Lime.

## CAMPHOR.

**Camphor Production.**—The leaves are the best parts of the tree to use. Yield 1% or more of crude Camphor.—Schimmell's Rep., Oct. 1912, Y.B.P. 1913,70.

**Camphor Estimation** (in Spirit of Camphor). Place 10 Cc. in a conical flask (= 1 Gm. Camphor) and add 4 volumes of Lead Subacetate Solution (Sp. Gr. 1.320) and shake. The Camphor collects as a cake on the top. The liquid contains some more in suspension. Filter in a cool place (covered). Wash flask with Ether and pour this on the filter, then wash with more Ether until all Camphor is extracted, collect Solution in a tared dish. Evaporate spontaneously, place in desiccator and weigh.—P.J. ii./13,881.

**Camsal.**—A microscopic mounting medium of Camphor and Salol.

**Euparal.**—A mixture of Camsal, Sandarac, Eucalyptol and Paraldehyde.—L.ii./13,1557.

**Artificial Camphor** has been manufactured by acting on turpentine with various acids.

The possibility of competing with ordinary Japanese camphor depends on the market value of turpentine. Pinene ( $\text{C}_{10}\text{H}_{16}$ ) is obtained by fractional distillation of oil of turpentine previously freed from resin. The pinene saturated with dry hydrochloric acid is the old-fashioned artificial camphor. The subsequent processes consist of splitting off the hydrochloric acid to obtain camphene, which is isomorphous with pinene. This substance, dissolved in glacial acetic acid, with a little sulphuric acid, yields bornyl acetate, and this saponified becomes borneol, which is identical with Borneo camphor. After oxidation synthetic camphor results, and this corresponds exactly with the Japanese and Chinese camphor, except in optical properties.—Houseman.

The synthetic is optically inactive, therefore is strictly not official. The *Off.* body is dextrorotatory, and a test for Artificial Camphor is also given in Spiritus Camphoræ. Synthetic Camphor has M.Pt.  $165^\circ \text{C}$ ., whilst natural has M.Pt.  $175^\circ \text{C}$ .—*c.f.*, also Ph. Ital.

A number of Patents for making.—Am. Jl. Ph., Aug. 07,349.

## CANNABIS INDICA (*Off.*).

Has been imported from East Africa to avoid the Indian duty. It is not so effective as the Indian. The extractive is about the same, but it contains less resin. The physiological test is the only safe one. Foreign cigarettes frequently adulterated with Indian hemp, in the paper and the gun,—needs verification.—Holmes, P.J. ii./09,132.

*Off.* requires that the drug should yield not less than  $12\frac{1}{2}\%$  extract to 90% alcohol and Ash not more than 15%.

A pharmacological study of *C. Americana*, i.e., *C. Sativa* grown in America—it is quite as active as that imported. Determination of physiological activity



by internal administration to selected dogs is reliable when the standard dose 0.010 per kilo body weight, is tested in comparison with the same quantity of a preparation of known strength.—Am. Jl. Ph., Jan. '08, 20.

### **Physiological Examination.**

"Intelligent fox-terriers" required for the experiments. It was found that activity was small in the case of some extracts yielding 34% insoluble residue in 90% alcohol, whilst every extract with insoluble residue not exceeding 2% was active.—Martin.—C.D. ii./09, 213.

The determination of the Iodine Number of fractional distillates, though advocated as a method of determining activity of a sample, is of no certain value as a means of estimating pharmacological activity, and hence is unsuitable as a substitute for physiological standardisation.—B.M.J. i./11 1171; P.J. i./11, 739; C.D. i./11, 854.

Charas is an intoxicating resinous substance secreted in the upper leaves and flowering spikes. Enzymes decompose Cannabis. Recommendation to import alcoholic extract in small sealed bottles. Production, adulteration, valuation, etc.—P.J. ii./08, 80, 347, 405.

### **CANTHARIS.**

Cantharides should contain not less than 0.5% Cantharidin.—P.G. has 0.8%. FR. CX. 0.4%.

Four samples of Russian and one of Spanish yielded 0.67 to 0.81% Cantharidin.—P.J. ii./04, 475.

Assay process (Greenish); by extraction with benzene.—P.J. i./07, 322 *et seq.*

Gaze's Assay process for galenical preparations of the drug: 50 Cc. of (for example) the tincture is evaporated to dryness with 25 Cc. of water and 1 Cc. of a 30% solution of Sodium Carbonate. The residue is taken up with 10 Cc. of water and 2 Cc. of 25% hydrochloric acid, the liquid transferred to a small separator and extracted with four separate portions of 10, 5, 5, and 5 Cc. of chloroform. The chloroform is evaporated at a low temperature, and the residue allowed to stand at ordinary temperature for twelve hours. It is then treated with two successive small portions of petroleum ether, each being poured on to a small filter, the residue and the filter washed first with water containing a trace of ammonium carbonate, then with pure water, and then dried at 50°. The portion remaining undissolved in the flask is treated with warm acetone, which is passed through the filter, which is further washed with acetone, and the brownish residue is dried on a water-bath to constant temperature and weighed. ("Apotheker Zeitung," 1911, p. 332, per C.D.).

### **CAOUTCHOUC.**

For India Rubber and substitutes, Properties and analysis, see Allen, 4th Edn., 1911, Vol. IV., 105—161, Gutta Percha (*ibid.* p. 156—161).

For latest information on Rubber from cultural, etc., aspect, consult works advised by the "India Rubber Journal," London.

Rubber substitutes.—See Nature, Mar. 17, 1910, p. 71.

**Synthetic Rubber.**—Processes of manufacture depend on polymerising isoprene. According to Harries (C.D. i./10, 121), this is effected by heating with Glacial Acetic Acid in closed containers to above 100° C.

India rubber is a condensation product of  $C_{10}H_{16}$ . This group is common to Turpentine and the Terpenes, in many essential oils. Synthetic Camphor is made from Turpentine. Synthetic Rubber has been made from  $C_{10}H_{16}$ , in some form or other. Nature elaborates many useful things from this base.—L. i./12, 595.

### **CASCARA SAGRADA.**

Tschirch has isolated a principle anthra-gluco-sagradin, and similar principles from Rhubarb, Senna and Rhamnus.

Oxymethylantraquinones are characteristic constituents of purgative drugs from widely separated natural orders, e.g., Rhamnus (*Rhamnaceæ*), Cassia (*Leguminosæ*), Quassia (*Simarubaceæ*), Aloe (*Liliaceæ*).—Tschirch, P.J. ii./09, 421.

The characteristic aperient action is not due to Emodin. Emodin is, however, a constituent, but chrysophanic acid or chrysarobin could not be found. Apparently no chemical differences between one and three year old ('matured')

bark. This was said to exhaust a ferment and to moderate the griping action which the fresh bark possesses.—B. & C.D. ii./04,268.

Assay of the oxymethylantraquinone drugs.—Tschirch, P.J. ii./05,225,248.

Further methods of determination on colorimetric principles.—P.J. ii./05,229.

Cascara glucoside,—a patented method of extraction.—P.J. ii./09,696.

The *refractive indices* of commercial fluid extracts of Cascara Sagrada found to agree with the specific gravity and amount of extractive. The refractive index would be useful in indicating that the extractive of galenicals is free from extraneous matter.—C.D. ii./09,185.

The medullary ray cells in *Rhamnus Purshiana*. Microscopic investigation.—H. Kraemer, Am. Jl. Ph., Sept., 1912.

## CERIUM. Ce=140·25 I. Wts.

This element, in addition to lanthanum and didymium, occurs as silicate in Cerite and as phosphate in Monazite, also in Samarskite and Gadolinite. Monazite is a mineral of fairly wide distribution in Brazil (in the State of Rio de Janeiro). For commercial details *vide* P.J. ii./09,492. Cerium has Sp. Gr. 6·7, Lanthanum 6·1, and Didymium 6·5. The last mentioned has been split up into Praseodymium = 140·6 (I. Wts.), and Neodymium = 144·3 (I. Wts.). Cerium possesses a variable valency. It is, like aluminium, either trivalent, or in some compounds apparently tetravalent, or even hexavalent as in the peroxide  $\text{CeO}_3$ , in this respect differing from the majority of the rarer earth metals and resembling the elements which are known to possess physiological action, for example iron, arsenic, antimony and iodine. Cerium oxide is contained in incandescent gaslight mantles. The filament in Nernst lamps is said to contain zirconia and yttria.

RUTILE is the ore Titanium Dioxide used in leather dyeing.—C.D.

The best result in manufacture of Titanium Metal was obtained by reducing Titanium Chloride ( $\text{TiCl}_4$ ) with Sodium by heat in a steel bomb. Titanium, practically 100% pure, was obtained. Sp. Gr. of the metal is 4·5 (Moissan found 4·87). It is brittle in large pieces when cold, but is remarkably malleable at a dull red heat.—Chem. News, May 20, 1910,232.

*For details of Cerium Oxalate, Sulphocarbonate, etc., vide Vol. 1, p. 813.*

## CHLOROFORM.

A. D. Waller by experiments on striated muscle states that the physiological power of chloroform is 12 times that of ether and 100 times that of alcohol.—Proc. Phys. Soc., Dec. 1908. L. ii./09,369.

Books give three different equations to represent the reaction between Chlorinated Lime and Alcohol. The one in which three molecules of alcohol yield two of Chloroform agrees best with practice.—C.D. Feb. '08. The method of manufacture is now so perfected that we may safely say it is almost impossible to purchase impure "Chloroform for Anæsthesia"—a number of tests have, therefore, been omitted.—*Vide* B.P.

In determination of the **Boiling Point** of chloroform it is important to transfer about the last 15% in the flask into a smaller flask or tube, otherwise it will be found in practice that this portion may refuse to pass over below 65 to 70° C.

*Test for Decomposition of Chloroform :—*

Small pieces of Pith steeped in Congo Red Solution. Acidity would cause the Congo Red dye to change to blue.—L. i./07,1033.

The drug is stated to be absorbed by the corpuscles rather than by the plasma of the blood. 'Carius' analyses best for estimating.—In chloroform narcosis the transport of chloroform from and to the lungs is a function of the red corpuscles.—Na. Jan. 9/08 (B.M.A. Inquiry).

## CHRYSAROBINUM.

May be converted into Chrysophanic Acid  $\text{C}_{14}\text{H}_5(\text{CH}_3)(\text{OH})_2\text{O}_2=204\cdot08$  I. Wts. by oxidation in alkaline solution and subsequent precipitation of the acid :  $\text{C}_{30}\text{H}_{26}\text{O}_7 + 2\text{O}_2 = 2\text{C}_{14}\text{H}_5(\text{CH}_3)(\text{OH})_2\text{O}_2 + 3\text{H}_2\text{O}$ .

Prof. Unna finds that the oxidation of chrysarobin when same is applied for healing upon the skin is due to the presence of oleic acid on the skin surface and the product formed is the remedial agent. He states that he proved that oleic acid present was sufficient to oxidise chrysarobin. This was facilitate



by the discovery that chrysarobin dissolved in benzol has a characteristic spectrum, which, during oxidation, also changes. It is characterised by two bands in the green lying closely together (535 and 510). If, however, the chrysarobin is oxidised in absence of alkalies, the spectrum shows only a broad indistinct band in the green and an obscuration in the yellow. This new body is to be called *oxychrysarobin* until its exact constitution is known. If we oxidise chrysarobin by means of oleic acid which has been in contact with air for some time, or by heated linseed oil (*siccatis*), by benzoyl peroxide by oleate of lead, or by persulphate of ammonia, oxychrysarobin in increasing degree results. If air is passed, on the other hand, through an alkaline solution of chrysarobin, we get chrysophanates; but if this be continued for a long time the change goes further, and finally, after adding acids, we get another product, easily soluble in benzol, which has also a characteristic spectrum—namely, an indistinct band in the green and chiefly a dark, sharply defined band in the red (625): this product to be called '*Chrysaloxin*.' It is recommended that for a quick and thorough treatment of psoriasis chrysarobin *siccatis* and ointments containing, besides chrysarobin, oleate of lead, should be freely used.—B.M.J. ii./10,1593.

### CINCHONÆ CORTEX.

The cultivation of the Cinchonas is carried on in India, in the Nilgiri Hills in the south, and near Darjeeling in the north-east, also in Ceylon, Java, and Jamaica.

The species *C. succirubra* has proved to be the hardiest and most easily propagated, and although on analysis the yield of cinchonidine and quinidine generally preponderates over that of quinine, yet the total yield—often up to 10%—of alkaloids from the bark of this Cinchona is very large (especially in the hybrids with *C. officinalis*); latterly the proportion of quinine in it has increased.

By far the largest proportion of the barks worked for quinine is Java *Ledgeriana* bark, all derived from the packet of seed obtained from one great tree by the Indian Manuel, and brought over by Ledger, which cost the Dutch Government £50 and Manuel his life. Of this bark Java produces nine to ten millions of pounds per annum, average test over 6% of sulphate of quinine, exceptional samples testing 10 to 12%. Much smaller quantities of *Calisaya* from South America, *Officinalis* from India and Ceylon, and *Succirubra* from India, Ceylon and Java, are also used, the latter being sought after by manufacturers of Pharmacopœia Germanica II. Quinine, which allows 10% or thereabout of Cinchonidine. Java Bark is year by year increasing in alkaloid content.—(Howard).

Note on a spurious reaction for cellulose and Cinchona Bark—a correction of Batka's test.—P.J. i./12,30.

Assay Methods.—Gadd, P.J. ii./05,579. Cæsar and Loretz's.—C.D. i./08,21.

#### Alpha Naphthol Test for Cinchona Alkaloids.—

Added to an Aqueous Solution of Quinine Sulphate, a few drops of fresh saturated alcoholic Alpha Naphthol Solution to which a few drops of Concentrated Sulphuric Acid (2 drops per Cc.) have been added, produces a yellow precipitate, when Reagent is in excess a yellow solution results. Quinidine, Cinchonidine and Cinchonine Sulphates act likewise. No other white alkaloids appear to give it. Cinchona alkaloids can thus be detected in presence of Atropine, Morphine, Cocaine, Strychnine, Caffeine, Brucine, Codeine and Antipryine. A drop of the Reagent added to Chloroform or Ether residues of any of the Cinchona alkaloids gives yellow colour. We tried this test and found it worked satisfactorily.—Watson, Am. Jl. Ph. 1913,502; P.J. ii./13,881; C.D. i./14,84.

#### Extractum Cinchonæ Liquidum (*Off.*).

Cinchona does not extract so readily with acetic acid as with alcohol and glycerin, but it gives a more permanent extract.—P.J. ii./09,142.

Methods of assay.—P.J. i./03,268; Y.B.P., 1902, 55,56. Useful suggestion for the U.S. method, Am. Jl. Ph. 1906,454. Use of alcoholic potash solution in place of aqueous.—P.J. ii./01,90; P.J. ii./05,124. Various methods of making Liquid Extracts of Cinchona discussed: that of Wobbe having advantage of small quantity of liquor and rapid percolation; the extract does not deposit.—P.J. i./04,324.

## CINNAMOMI OLEUM (*Off.*).

A test to ensure absence of cinnamon-leaf and cassia oils is given—*Off.* Further, it should now contain 55 to 65% of cinnamic aldehyde as determined by a sodium sulphite addition process.

The Bisulphite method is more commonly used, *c.f.* other Pharmacopœias — Parry.

See also note on Bark oil: Recent experiments in distilling show that Sp. Gr. higher than 1.016 could not be obtained. Opinion is expressed that the characters hitherto accepted for the oil have not been based on normal distillates.—P.J.ii./10,145.

There is no difficulty in obtaining shipment of Cassia Oil with over 90% Cinnamic Aldehyde. Practically all the oil of 80 to 85% is adulterated with Resin or something similar.—P.R., Dec., 1913,402.

## CITRONELLÆ OLEUM.

Genuine Oil from Ceylon Government gave the following figures:—Sp. Gr. at 15.5° C., 0.884. Optical rotation—3.3, Citronellal 36%, Geraniol 41%. Schimmel's Test. Turbid solution.—C.D. i./06,355. See also P.J. ii./08,623

Citronella Oil with Carbolic Acid acts admirably in driving off mosquitos. (Cairo).—Ph. Notes.

The tse-tse fly has marked repugnancy to the plant.—L. i./09,701 (*c.f.* trypanosomiasis) but it has been tried (L. ii./09,1197) and has lost its reputation as a means of warding off the insect—the odour of the oil is not given off without bruising the plant.

Citronellol and Citronellal described, see Allen, 4th Edn., 1911, Vol. IV., p. 263-269.

The *Perfumery Record* (Nov. 1911) criticises Schimmel's 'Test' for Citronella Oil as contained in their Report. This test is arbitrary and not to be compared with an Acetylising method. Schimmel thinks that no water is formed in the acetylation of Geraniol. Dry, *i.e.*, Fused Sodium Acetate is, however, always employed for the purpose.  $2ROH + (CH_3CO)_2O = 2 RO(OCCH_3) + H_2O$ . Schimmel maintains on the other hand that the action of Sodium Acetate is a catalytic one.—C.D. ii./11,787. See also P.R., 1913,167; Y.B.P. 1913,75.

## COAL TAR DERIVATIVES.

### Methylene Blue (Medicinal).

N.B.—Distinguish carefully from the commercial article containing zinc chloride. U.S. provides special tests. Medicinal Methylene blue is preferable to the commercial for making alcoholic solutions, as being more soluble for bacteriological staining, *c.f.*, Löffler's Alkaline Methylene Blue.

#### Methylene Blue as Indicator in Iodometric Titrations.

When titrating with standard iodine, the usual starch indicator may be replaced by methylene blue. Use a solution of 0.05 Gm. in Water 1,000 Cc. 1 Cc. of this is added to 50 Cc. of the solution to be titrated. The end point is the change from blue to yellowish-green.—J.C.S.A. ii./10,747. An indicator is hardly necessary in Iodometric titrations.

### TESTS FOR PERMEABILITY OF THE KIDNEY.

**Methylene Blue Test.**—1 Cc. of 1 in 20 solution is injected into the gluteus maximus and the urine is turned pale green. Sterules of this strength are prepared.

Discussion on the elimination of Methylene Blue.—Chromogen usually appears in 15 minutes, the blue in 30 minutes.—L. i./07,711.

The method is sufficient to compare the work of the two kidneys. Both the Methylene Blue and Phloridzin test are trustworthy.—L. i./07,795.

Certain organs become blue while others remain normal colour. Reduction is going on in the latter, as Methylene Blue is decolourised when reduced.—L. i./07,784.

To determine functional condition of the stomach caoutchouc membrane capsule of  $\frac{3}{4}$  grain.—L. i./08,1292.



Methylene Blue has also been used in place of Ehrlich's diazo-reaction to indicate the presence or absence of typhoid, measles, smallpox, or phthisis; these diseases cause the urine to assume a green colour when 4 drops of 0.1% solution are added to 4 or 5 Cc. urine.—M. 1905.

### Indigo-Carmine Solution 0.4%.

20 Cc. of 0.4% Solution (i.e., 0.08 Gm.) of Indigo Carmine injected intramuscularly,—colour should appear in the urine in 10 to 12 minutes if functional capacity is in order.—B.M.J. i./08,89. We suggest that the 0.08 Gm. should be dissolved in a *less quantity of water*.—e.g., 5 Cc. This forms a practically saturated solution (1 in 60). Previously a stronger solution (4%) was advised but this is unattainable.

Cystoscopic examination of the urethral openings and the urine gives by depth of colour, indication of renal functional power.—L. i./07,793.

**Sahli's Pill.**—To diagnose peptic activity of the gastric juice a pill of Methylene Blue is enclosed in catgut in the form of a so-called oesmoid pocket and swallowed by the patient after dinner. As soon as the catgut is dissolved Methylene Blue escapes and dyes the urine, the time required to effect this result furnishing a measure of the condition of the gastric secretion. The Methylene Blue may be enclosed in a small piece of rubber tubing tied with thin catgut—the knot being touched with shellac.

Indigo or Indigotin (natural) is obtained from the shoots of *Indigofera Tinctoria* (*Leguminosæ*) in India and Java, by maceration with lime and water. The pure substance has the composition  $C_{10}H_{10}N_2O_2$ . For chemical synthesis, v.p. 241.

Indigo Carmine is stated to be the Sodium Salt of Disulphindigotic Acid (which acid substance is Sulphate of Indigo, or Soluble Indigo) prepared by adding gradually Powdered Indigo 1 to Nordhausen Sulphuric Acid 5 or Oil of Vitriol 8—the vessel being kept surrounded by cold water.

Indigo Soluble. FR. CX. has *Syn.* Sodium INDIGO-DI-SULPHONATE, INDIGO CARMIN, CERULEINUM.

$Na. SO_3. C_6H_3 < \begin{smallmatrix} CO \\ NH \end{smallmatrix} > C=C < \begin{smallmatrix} CO \\ NH \end{smallmatrix} > C_6H_3. SO_3. Na = 466.224$   
I. Wts.

Completely *soluble* in warm but only slightly in cold water. Soluble Indigo as mostly understood is the acid substance not the sodium salt.

The Sodium Salt is formed as a precipitate on neutralising Soluble Indigo with a Sodium Salt. It has to be washed with a solution of the same salt—to remove excess of Sulphate of Indigo. The product is pressed and dried and is then soluble in water.

**Phloridzin Test.**—This consists in injecting 5 mgr. of phloridzin (*q.v.*) subcutaneously in 20 to 30 minims of water. Glucose should normally appear in the urine in half-an-hour.—M.A. 1904,461,462.

For determining the diseased side of the kidney this test is frequently more delicate than the others.—L. i./07,797.

For kidney examination the technique of Caspar's method which consists in the subcutaneous injection of 1 Gm. of 1% Phloridzin Solution and observation as to (a) excretion as sugar by a healthy kidney or (b) non-excretion at all or more slowly and to less extent (diseased) is described. This test as a rule exceeds the carmine blue test in delicacy, especially where pyelitis is present.—B.M.J. ii./08,998.

0.01 Gm. of phloridzin injected into the buttock will cause excretion of glucose 10 to 15 minutes afterwards. In extensive disease of the kidney the excretion is delayed or absent. In health it may also be delayed 30 minutes.—B.M.J.E. ii./09,22.

**Phenolsulphonephthalein**  $C_6H_4 \begin{matrix} \nearrow SO_2 \\ \searrow C \end{matrix} O : (C_6H_4OH)_2 = 354.182 \text{ I. Wts.}$

A red crystalline substance slightly soluble in water, more soluble in Alcohol, insoluble in Ether. With alkalis it gives an intense purple red colour even in extreme dilutions..

**Manufacture.**—It may be prepared from Saccharin by hydrolysis and subsequent treatment of the anhydride of Sulphobenzoic Acid obtained therefrom with Phenol. *e.g.*, Saccharin 100 Gm. boiled with 1500 Cc. of water and 125 Cc. Concentrated Hydrochloric Acid until no longer sweet (4 to 6 hours), then evaporate to crystallise, collect crystals and evaporate the mother liquor to almost dryness and collect the crystals and dry them with the others. Distil the dried crystals thus obtained with an equal weight of  $P_2O_5$ , this gives the anhydride of *o*-Sulphobenzoic Acid which is then fused with Phenol at  $130^\circ \text{C.}$  for several hours until combination is complete.—L. G. Rowntree and J. T. Geraghty, *Jl. Pharm. and Exptl. Therapeutics.*—Vol. i./1909-1910, p. 579.

### Phenolsulphonephthalein Test,—Technique.

An aid in proving whether the diminished excretion of Nitrogen is due to interference with function and also as a guide to the degree of interference with renal function in toxæmia of pregnancy and threatened eclampsia.

Give 300 to 400 Cc. of water half an hour prior to the test. Empty the bladder with a catheter and give subcutaneously in the upper arm 6 mgr. of Phenolsulphonephthalein neutralised with Sodium Hydrate in 1 Cc. of water ('Sterules' of this strength are made).

Then allow the urine to drain through the catheter into a test tube containing a drop of 25% *Sodium Hydrate Solution* and note the time of the appearance of the first pink tinge. Remove the catheter and determine colorimetrically the amount of the body excreted in the first and the second hour. Normally the drug appears in the urine in from 5 to 11 minutes and in the first hour from 38 to 60%, and in the second 22 to 25% are excreted. In severe, acute nephritis the permeability is markedly decreased, also in chronic interstitial nephritis. The delayed appearance and especially the diminished excretion in the two hour period are more accurate indications of functional derangement than an estimation of total solids or Nitrogen.

In 18 clinically normal pregnancies there was a relatively diminished excretion (*i.e.*, interference with renal function) as compared with that in normal non-pregnant cases. These data suggest that the depression in Nitrogen secretion in late pregnancy is due to interference in renal function and in absence of actual renal lesions the cause may be disturbed circulation due to pressure of the gravid uterus.—*B.M.J.E.* i./13,75.

Further report says, the rate of excretion is of less importance than the relative quantity excreted by each kidney and the fact whether the whole amount is excreted. The urinary pigment may be overcome by precipitating with Lead Acetate.—*B.M.J.E.*, 1./13,80.

Other observers require three hours as time. 60% should be excreted in this period.—*M.* 1912.

### Phenacetinum.

**Manufacture.**—For notes on the process of manufacture of Phenacetin whereby one molecule of para-nitrophenol is made to yield a large number of Phenacetin molecules, *vide* May, p. 71.

The action of Anilin and Paraminophenol derivatives is within limits proportional to the amount of Anilin, Paraminophenol or Phenetidine formed in the organism. Several more soluble derivatives of Phenacetin have been made, *e.g.*, by introducing Sulphonic for Carboxylic radicals, but these only tend to spoil the physiological action.—May, *c.f.*, also Lactyl-Phenetidine—the Lactyl analogue of the body under consideration.

Cold saturated solution treated with bromine water should not become turbid (absence of acetanilide, B.P. & U.S.) 0.1 Gm. boiled one minute with 3 Cc. of sodium hydroxide solution 1 in 2, and the solution cooled and shaken with 5 Cc. of chlorinated soda solution, a clear yellow liquid is produced (absence of acetanilide, U.S.).

Determination of Phenacetin or Acetanilide in complex mixtures.—*Am. Jl. Ph. April*, 1907; *P.J.* i./07,521.



## COCÆ FOLIA.

**Assay.**—Our examination of eight commercial samples of Coca leaves recently by the U.S.P. assay method, showed Ether-soluble alkaloids varying from 0.51-1.10% by titration and from 0.38 to 1.10% by weight. The highest average percentage of Ether-soluble alkaloid was obtained from small yellowish leaves, whilst the lowest average was given by large leaves the former resembled Peruvian and the latter Bolivian Coca.

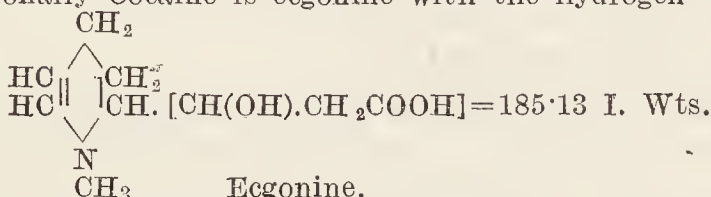
*E. Novogranatense* (Java Coca) plants give good yield. 100 plants yield 2.00 kilos of dry leaves whilst the same number of *E. Coca* yield only 0.262 kilos, but further experiments will be tried on this subject. Supplies of Coca from Java and Ceylon tend to diminish output in Peru and Bolivia.—Bulletin of the Imperial Institute per C.D.

### Fluidextractum Cocæ U.S.

In the U.S. assay three extractions should be made with both the ether and the acid liquid. Titrate with  $\frac{1}{2}$ N/20 solutions.—C.D. ii./o8,493.

## COCAINA.

Constitutionally Cocaine is ecgonine with the hydrogen



Ecgonine.

atoms in the carboxyl and hydroxyl groups replaced by a methyl and benzoyl group respectively; produces an anæsthetic effect on the tongue.

For further details consult Gordon Sharp.—P.J. i./o9,184.—‘Coca and Cocaine studied historically.’—*Vide* also *ibid*, p. 356 for the synthesis of the racemic modification corresponding—physiologically and chemically—to natural cocaine by Willstätter.

For a résumé of the chemistry of this and other local anæsthetics, see Fourneau, *Int. Cong.*, 1909.

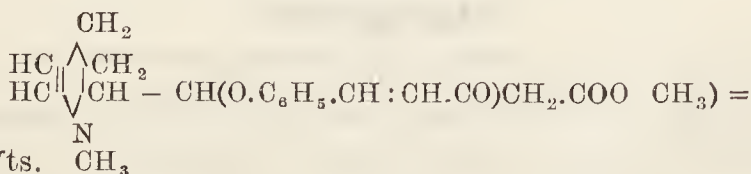
**Toxicology.**—Is converted into ecgonine in the organism. Methods of detection.—Y.B.P., 1902,60.

A Cocaine Salt in solution may be estimated by precipitating Cocaine periodide with decinormal Iodine.—P.J. i./o1,553,602; ii./o1,223,254.

**PERMANGANATE TEST FOR COCAINE AND OTHER BODIES.** When a drop of a Solution of Cocaine is placed on a dried film formed by a Solution of Potassium Permanganate on a micro slide and examined under the microscope, oily drops are seen. If however, the Cocaine is dissolved in a Saturated Solution of Alum, crystals of Cocaine Permanganate will be quickly observed. Alypin, Tropacocaine and Scopolamine produce crystals from Aqueous Solutions. Beta-Eucaine, Stovaine, Novocain, Holocain and Nirvanin form no crystals with Permanganate. Saporetti’s Bromine Test distinguishes these latter for which *vide*.—P.J.i./II,94.

With Chromic Acid and Cobalt Nitrate Alypin behaves similar to Cocaine and Eucaine and precipitates with usual alkaloidal reagents and caustic and carbonated fixed alkali and with ammonia.—B.M.J. i./o7,87.

The four alkaloids Cocaine, Truxilline  $\text{C}_{19}\text{H}_{23}\text{NO}_4 = 329.194$  I.Wts. (previously called Cocamine or Isatropylcocaine), Cinnamyl-cocaine



329.194 I.Wts.  $\text{CH}_3$

and Tropa-cocaine  $\text{C}_8\text{H}_{14}\text{NO}\cdot\text{C}_6\text{H}_5\text{CO} = 245.162$  I. Wts. are known to exist in coca leaves.

Cocaine, truxilline and cinnamyl-cocaine being ecgonine derivatives yield ecgonine, acids, and methyl alcohol on hydrolysis. This fact is of importance commercially as the amorphous residue remaining after extracting as much as possible of the crystalline cocaine can be converted into ecgonine, and this by

treatment with benzoic anhydride and methyl alcohol can be converted synthetically into cocaine.

Although formerly care was taken in the extraction to preserve the Cocaine now-a-days manufacturers rely on the ecgonine content. After isolation in the crude the 'Cocaine' is treated so to reintroduce the methyl and benzoyl group. Process for ecgonine estimation has been devised.—Am. Jl. Ph. Feb. '08. p. 74.

Methods of assay.—P.J. ii./03,784; C.D. ii./03,800; P.J. ii./05,724.

Cocaine volatilises at 100° C. This is of importance to recollect in analytical work.—Am. Jl. Ph., Dec. 1910, p. 576.

### **Cocainæ Hydrochloridum.**

It should not only be in good crystals, but should, by the following modification of **MacLagan's Test**, yield a distinctly crystalline precipitate of pure Cocaine within three minutes—when 1 grain of it dissolved in 2 ounces of distilled water, and six to eight drops of solution of ammonia, B.P., are added and well stirred. If more than 4% of amorphous alkaloid (principally Truxilline) be present, there will be only a cloudiness. The precipitate re-dissolves after twenty-four hours or more, the Cocaine being converted into methyl alcohol and benzoyl-ecgonine. Truxilline is highly toxic. (CODEX also gives this test and states the same. P.G.V. gives it slightly modified.)

### ***Can Cocaine Hydrochloride Solutions be sterilised by boiling with impunity?***

Statements to the effect that Cocaine would be decomposed in solution on boiling (c.f. B.M.J. i./09,783) probably depend on the slight alkalinity of the glass. A temperature of 100° C. on the water-bath in glass vessels causes only the barest trace of decomposition.—P.J. ii./09,36; ii./09,124.

With a view of settling the question, we provided S. Stephenson with 2 solutions 2% strength, one boiled with the Cocaine in, and made up to strength again, and the other made with ordinary aseptic precautions, but not boiled with the Cocaine in it. He reports:—"These solutions labelled simply 'A' and 'B,' without any further indication were tried on 10 eyes belonging to 5 persons. I could make out no difference as regards powers of producing local anæsthesia of conjunctiva and cornea between them. I am decidedly of opinion that such boiling as is sufficient for sterilisation does not impair the anæsthetic action."

Merck had previously conducted experiments on this matter and came to similar conclusions. *Surgeons may therefore use sterilised solutions with perfect safety.* C.f. Edn. XIV., p. 262.

### **Spinal Anaesthesia with Stovaine.**

Examination of urine and liquor cerebri for Stovaine eliminated, Barker describes extraction method with Ether and testing the Hydrochloric Acid solution of the base with dilute Iodine Solution,—the brick-red precipitate is indicated with so small a quantity as 1 in 150,000. N.B.—It is important to drive off the Ether from the Hydrochloric Acid Solution, otherwise precipitate will be given whether Stovaine is there or not. Liquor Iodi more delicate than Mayer's Reagent.

The investigation showed that long after the analgesic effect of Stovaine (1 to 2 hours) had subsided, the base of Stovaine remains in the cerebro-spinal fluid—even for 24 hours. Stovaine (Hydrochloride) is apparently the anæsthetic substance, which is split up by the alkaline fluid.—B.M.J. ii./09, 789, *et seq.*

## **COLCHICUM.**

The corms are said to be  $\frac{1}{3}$  weaker in alkaloid than the seeds.—Y.B. P./02,171, about 0.3 to 0.8% is found in both.—P.J. i./04,5,246.

Historical study. Colchicum is derived from Colchis, a district in Asia Minor.—P.J. ii./09,5.

Acetic Acid nearly equal to Proof Spirit to extract Corm and Seed.—P.J. ii./09,142.

Professor La Wall wishes the man who invented the *U.S. Assay* process for Colchicum Corm had to use it continually to earn his living.—Am. Jl. Ph., Feb./08,76.

Farr and Wright devised a process employing Iodine as precipitant, shaking out after with Chloroform in presence of Sulphuric Acid.—P.J. ii./10,579.



**Fluidextractum Colchici Seminis. U.S.**

In the U.S. Assay the aqueous solution of colchicine should be filtered through cotton-wool and washed once with 10 Cc. of petroleum ether to extract the last traces of fat. The alkaloid extracted by chloroform should be entirely soluble in water.—C.D. ii./08,493.

**CONIUM.**

The amount of alkaloid found in the root, stem, and leaves is small, while in the fruit it is considerable during the period when the fruit is forming its reserve material, reaching as much as 3 per cent. or even more. When the fruit has finished forming its reserve and ripens the proportion of alkaloid is found to become less, not greater, until it falls to less than 1 per cent. in the ripe fruit. Moreover, the proportion of alkaloid to total nitrogen gradually diminishes as the fruit develops. If the alkaloid were a by-product as viewed by Pictet in the production of protein it might be expected to retain a fairly constant ratio, and not become a diminishing one.—E. H. Farr, Pres. Add. B.P. Conf., 1914, P.J. ii./14,117.

The *U.S. Assay Method* is not at all satisfactory. The ammonium sulphate formed in the process does not separate completely, and the neutralisation with sodium carbonate requires great care. The method given in the 1901 "B.P.C. Formulary" is more satisfactory.—C.D. ii./08,493.

**Characters and Color-Reactions of Conine, Conhydrine, Pseudo-conhydrine, Coniceine, and a new Conine isomer.**

*Conhydrine* stated to have an odour resembling the urine of mice. It is crystalline—either in plates like cholesterine, or in needles.

*Pseudoconhydrine* is isomeric with Conhydrine.

*Coniceine* is optically inactive. The Hydrochloride is hygroscopic.

There is no 'dry' reaction characteristic of Conine.—P.J., ii./09,34.

Reactions of Conine alkaloids in solution.—P.J. ii./09,70, *et seq.*

A scheme for differentiating Conine, Nicotine, Lobeline, Sparteine, the Conhydrines,  $\gamma$ Coniceine, and a new isomer is given.—P.J. ii./09,103; see also P.J. ii./05,333.

**CREOSOTUM.**

Ⓢ **Creosote.** According to FR. CX. consists of about half its bulk Creosote the other half consisting of Guaiacol with some cresylols, phlorol, or ortho-ethylphenol, etc. Easily soluble in alcohol, ether, anhydrous glycerin, chloroform, also in caustic potash and soda solutions, and in acetic acid (glacial). It distils between 200 and 220° C. U.S. (Revised) now omits glycerin test.

*Off.* and P.G.V.—Sp. Gr. not below 1.080. Distils between 200 and 220° C.

**Genuine Beechwood Creosote** yielded 39% Monophenols, 26.48% Guaiacol, 32.14% Creosol  $C_6H_3CH_3.OCH_3.OH$  and homologues, Pinewood Creosote about the same but 20.3% Guaiacol and 37.5% Creosol and homologues—all boiling between 200 and 210°C.—Am. Jl. Ph. 1899, pp. 409-413.

Allen, 4th Edn. Vol. III., p. 353, gives results of his own investigation and that of others in tabular form. The composition of Creosote varies considerably.

It is dextrorotatory—*Off.* (not *laevo* B.P., 1898), or is inactive (Umney).

**CUPRUM.**

For purifying water, Kraemer found that strips of copper foil placed in water containing colon and typhoid bacilli completely destroyed same in less than four hours. Considered a safe domestic method. A piece of copper foil  $3\frac{1}{2}$  inches square in a quart of water six hours or so is all that is necessary.

He also gives a table of figures showing the amount of copper normally present in a number of substances in mgr. per kilo:—Belladonna contained 4,200. Henbane 3,600.—Am. Jl. Ph., June 05,274.

A sample of milk in which copper was present to the extent of 1 in 2,000,000 kept longer than usual. Experiments showed small quantities of copper salts prevent putrefaction in egg and blood albumen, meat and other nitrogenous substances.—P.J. ii./10,392.

The lobster contains 0.002% metallic copper in the whole body.—P.J. i./11,405.

Chemical relationships of the copper fungicides—Nature, Mar. 3, 1910 p. 13.

## DIGITALIS FOLIA.

**Preservation.**—The dried leaves are best preserved in small containers over a layer of lime,—the freshly burnt quicklime being in a wide mouth bottle tied over with a layer of gauze.—*c.f.*, E. M. Holmes, P.J. i./11,164, and P.G.V., also Am. Jl. Ph., May, 1912, 201, *et seq.*

The freshly powdered leaf is favoured by many practitioners as the best method of giving the drug.

The recently issued new edition of *F. Norsk* advises leaves of the indigenous wild-growing flowering plant dried for five hours at about 80° C., filled into well-closed containers of not more than 50 Gm. The same rule applies to powdered Digitalis.

**Deterioration of Preparations** of Digitalis we deal with under ASSAY.

### Cultivation.

Tschirch pointed out that nothing was known as to the influence of the composition of the soil, of shade or light, of moisture or lack of moisture on the formation of Digitoxin in the plant.—P.J. ii./09,420.

Hale has disposed of the idea which has been promulgated that the leaves of wild plants are more potent than cultivated ones. Nevertheless some of the former, he says, are more potent than the latter but cultivation *per se* has nothing to do with the fact.—P.J. i./11,578.

Our own investigations have indicated that there is much to be learnt as to the ideal conditions for growth of Digitalis. Speaking generally, the author is of the opinion that a **dry season favours potency**. The most potent leaves in an extensive series that we have examined (both chemically and physiologically) were second year's leaves from plants grown in England in a sunny exposed situation. These leaves were from plants showing no flower spikes at time of collection. (NOTE.—*All second year's plants do not necessarily flower.* We lay more stress on the sunny situation than the point of non-flowering at the time.) See also Symes,—Footnote, p. 56.

Holmes, P. J., ii./05, p. 5, thought that Digitalis prefers a moderate amount of sun. Other workers in the past have expressed similar views. Ransom and Henderson found sunlight to influence the alkaloidal content of *Belladonna (q.v.)* which resembles Digitalis in nature in being a plant growing in semi-shade.

J. Bowmann (Schweiz Woch. Chem. u. Pharm., 1913, 51, 117, has determined that the yield of active principles from this (as also from Aconite, Belladonna, etc.), is proportional to fluctuations in temperature.—From the years 1907-1911 the lowest yield was the cold year 1909, and highest in the **warm** year 1911.

Details of experimental cultivation at Minnesota University. The petioles and midribs contain less of the active principles than the lamina—they can be removed by sifting. Moisture determinations of first year's leaves showed 85%. A review of literature to that date.—Am. Jl. Ph., May, 1912, 201, *et seq.*

It is held that **botanical** differences between Digitalis plants will account in part, at least, for differences of opinion as to first and second year's leaves and fresh and dry leaves. Importance of employing selected *heavy* seed for cultivation.—P.J. ii./12,368.

### First or Second Year's Leaves the best?

There is a good deal of divergence of opinion on this subject.

Physiological tests have determined second year's leaves to be somewhat stronger than the first—*i.e.* in proportion of 10 to 8½. The difference is probably due to the excess of petiole in the first year's growth which it may be noted in P.L. was ordered to be removed.—P.J. i./07,198, *vide* also Am. Jl. Ph., July/08,330.

Hale, on the other hand, states that he has found the first year leaves are from 28 to 40% more active than the best second year leaves procurable. The real cause of the variation in the potency of digitalis leaves seems to be connected with the nature of the soil and the character of the season, etc.—P.J. i./11,578.



Focke states that second year's leaves have their highest value at time of flowering and the first year's leaves attached to them the highest value in late summer.

Our own opinion is that there is probably little to choose between the activity of first and second year's leaves. The character of the season has much to do with the activity—a dry season will produce less yield of herb than a wet one, but an increased proportion of active glucosides.

A good practical paper on Digitalis:—First year's leaves are intensely bitter and a good Tincture can be made from them if collected in dry season and carefully dried. Further, though the B.P. directs to be collected at time of flowering, *i.e.*, in June or July (second year's growth), it was found that a good Tincture could be made from leaves collected as late as end of September.—P.J. i./11,102. See also several references on the same subject in 'Digitalis Assay' by the author, p. 20, *et seq.*

*D. gloxinceflora* a horticultural gloxinia-like strain of *D. purpurea* provides leaves approximating the latter in potency. Leaves collected from wild plants in the first year may be nearly or quite as active as second-year leaves.—F. A. Miller and W. F. Baker, Int. Cong. N.Y., 1912, per C.D. ii./12,482.

The first year's leaves (U.S.) show a higher percentage of glucosides than required by the U.S.P., hence should be admitted into that Pharmacopœia.—Am. Jl. Ph., Dec., 1912.

### Content of Active Constituents.—

Gordon Sharp and F. W. Branson found that leaves gathered in November are as active as those gathered in August and that leaves from plants that had flowered are equally as toxic as those from plants that had not yet flowered.—P.J. ii./12,131. See also B.M.J. ii./14,952.

The content in the leaf of Digitoxin is about 0.1 to 0.3%. It is most abundant in the leaves in August; hot dry weather increasing the content.—N.S.D.

Work in America shows 0.171 to 0.455%.—C.D. i./08,597.

First year's leaves in U.S.A. contained 0.3%.—Am. Jl. Ph., Dec., 1912.

The average therapeutic dose of Digitoxin may be regarded as 0.5 mgr., corresponding to the effects of 0.06 Gm. of Digitalis leaves—but this quantity of leaf would contain only 0.12 mgr., so there is a discrepancy of about 400%. Digitoxin therefore represents only about  $\frac{1}{4}$  the power of Digitalis. To assay Digitalis by Digitoxin alone would be about as rational as to assay Opium by Codeine content.—Am. Jl., Ph. Mar., /08, p. 108.

'Digitalic Acid.'—Regarded as the mother source of the Glucosides. Details of manufacture.—T. Stephenson, P.J. i./14,165,187.

## Characters and Tests of Glucosides.

The determination of the value of a Digitalis preparation (especially the Tincture) by chemical means is fraught with considerable difficulties owing to many factors, *e.g.*, the numerous glucosidal bodies contained, the fact that it is not possible to point to one glucoside as the potent constituent as representing the activity of the drug, and again the extraction of the substances in any degree of purity requires some analytical skill.

We adopted as our standard a Tincture having by physiological tests a M.L.D. calculated as 0.75 Cc. per 100 Gm. weight of frog.

In a paper read before the Pharmaceutical Society of Great Britain, Dec. 10/1912, the results of examination were provided of some two dozen samples of leaves both of the author's growing and from sources in various parts of the world (Great Britain, Germany, Italy, India, etc.). Almost all of these leaves gave tinctures of Standard or above Standard strength.—P.J. ii./12,745,758,778; L. ii./12,1740; B.M.J. i./13,28. The paper was published in booklet form entitled 'Digitalis Assay.'

The glucosidal bodies with which we are concerned are:—

### From Digitalis Leaves.

**Digitoxin** the most potent glucoside present.

**GITALIN** which is the name given by Kraft to DIGITALEIN of Schmiedeberg and Kiliani in a purified form.

**DIGITONIN AMORPH.** *Syn.* DIGITSAPONIN, Kraft.

**GITIN.**—A further Saponin.

The last two are relatively inactive.

### From Digitalis Seeds.

**Digitalin** (*Syn.* Digitalinum Verum).

**GITALIN.** Common to leaves and seeds *vide antea*.

**DIGITONIN AMORPH.** (Schmiedeberg) and **DIGITONIN CRYST.** of Kiliani.

In 'DIGITALIS ASSAY' we give a full account of the body Gitalin. The glucoside is to a great extent of academic interest rather than practical importance. The yield of it is stated to be about 0.07%.

Focke has recently reported on his experiments with gitalin, which is said to be present in what was considered as pure digitoxin to the extent of four-fifths, and he concludes from his experiments that a solution of gitalin could well serve as a standard for physiological assay.—C.D., Oct. ii./13, from "Zeitschrift für Experimentelle Pathologie und Therapie."

### Digitoxin Recognition Tests.

**Keller-Kiliani** (*Syn.* Keller's Test) for Digitoxin in the Leaves.—Shake 10 Cc. of filtered infusion in boiling water 1+20 in a separator for a few minutes with chloroform 10 Cc., add ether 5 Cc. and alcohol 5 Cc.; shake again and filter off the chloroform-ether solution through a filter moistened with chloroform. The liquid is evaporated and the residue dissolved in 3 Cc. of acetic acid (96%). A drop of diluted solution of ferric chloride (1+19) is added, and the whole in a narrow test-tube, is layered carefully upon sulphuric acid; at the point of contact of the two liquids a brownish-red zone develops, and over it a bluish-green zone.—P.G.V. We find in practice the presence of Chlorophyll hinders the colouration considerably.

The test may also be applied to the glucosidal substance *Digitoxin* thus:—Dissolve 0.001 Gm. in 3 Cc. Glacial Acetic Acid, add a few drops of the Ferric Chloride Solution and proceed exactly as the rest of the last mentioned.

It is held that Digitoxin produces blue in Acetic Acid in this test because it contains Digitoxose.—Am. Jl. Ph., May, 1913.

**Fröhde's Test** (Sulphuric Ammonium Molybdate *vide* Colorimetric Method *infra*) Ammonium Molybdate 1 *w/v*. in concentrated Sulphuric Acid used as a layering test, we found, is very characteristic for Digitoxin; used as a *mixing test* it is also very distinctive for Digitalin.

### Kiliani Test for Digitalin.

Ferric Sulphate 0.05 Gm. is dissolved in water 1 Cc., and Sulphuric Acid added to 100 Cc. Employed as a mixing test (0.1 mgr. of the glucoside is sufficient, dissolved in 0.2 Cc. of Glacial Acetic Acid), this reagent produces a pink coloration.

This test with *Digitoxin* produces a brownish colour—if pure a decided brown.

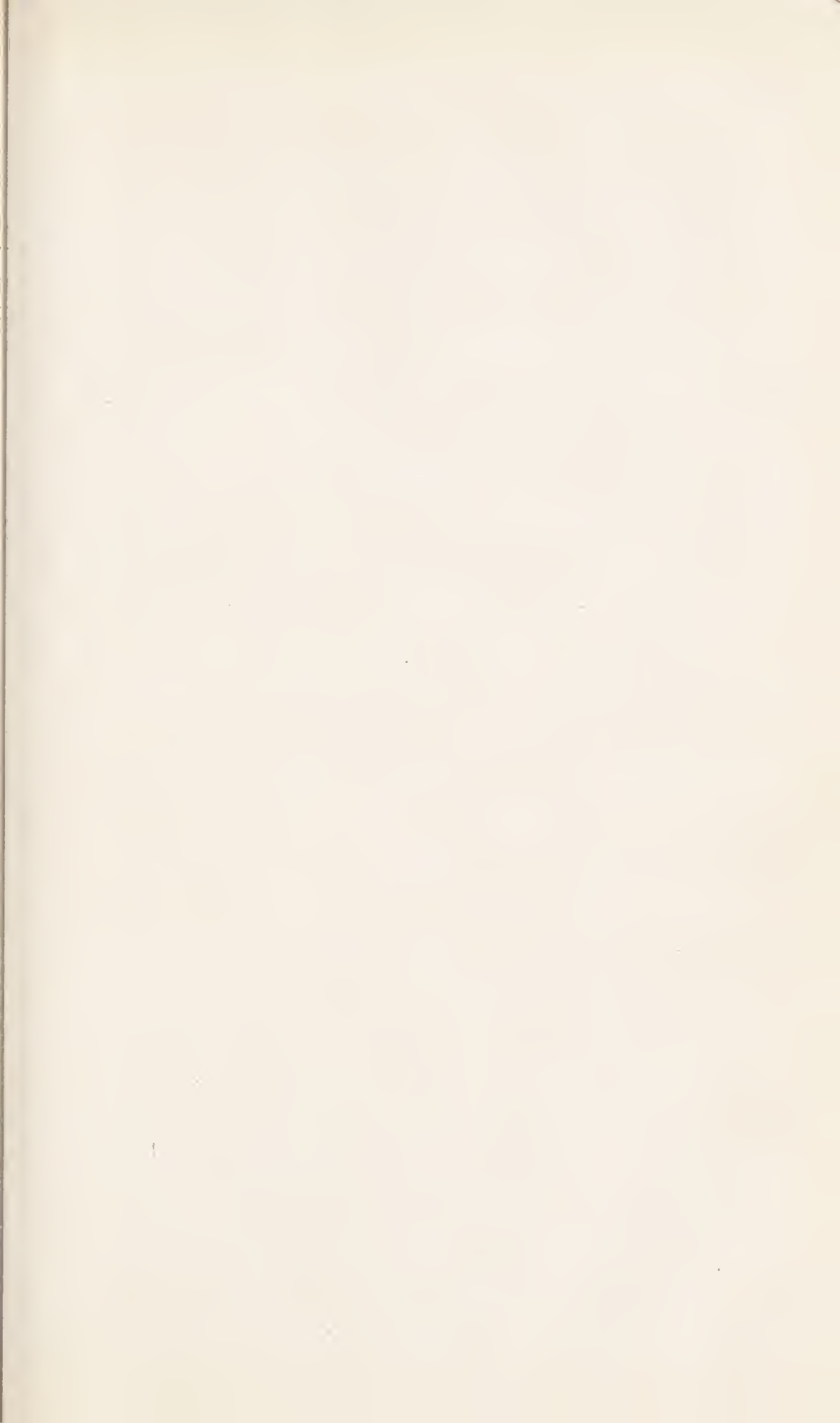
## Digitalis Assay.

**Chemical Assay processes** have been devised by many workers in the past. In this connection the names of Keller, Fromme, Stoeder, Gordon Sharp, Barger and Shaw, Barenstein and Burmann should be mentioned.

These methods were almost entirely centred on an estimation of the **Digitoxin** content—*whilst ignoring the bodies which are known to be readily soluble in water*. That this was fallacious was shown by Ziegenbein, who found that leaves containing only 0.125% of this glucoside were twice as active as those containing 0.226%.

Our aim was to produce a method which shall include these latter important substances in addition to Digitoxin or a closely allied body. The process devised effects this adequately and, it may be added, includes a strong indication of Digitoxin—either by reason of the actual solubility of this body in the repeated quantities of solvent prescribed (the amount of Digitoxin in 10 Cc. of Tincture is obviously extremely minute though sufficient to detect with the delicate reagent) or owing to the fact that Digitoxin is soluble in the presence of the other accompanying Glucosides, Saponins and decomposition products. The process does not claim to necessarily extract *all* the Digitoxin though *practically none can be found in the residues* in the various steps.





This simple Chemical Assay Method of the tincture is equivalent to and will supplant, if possible, the Physiological Assay Method based on the minimum lethal dose required to kill a frog and calculated to 100 Gm. body weight.

The **Colorimetric Method** devised requires some care in carrying out, as it is strictly quantitative. It is as follows:—

To determine whether a Tincture is up to Physiological Test requirements usually taken at M.L.D. = 0.75 Cc. per 100 Gm. body weight of frog) mix 10 Cc. of the Tincture with 10 Cc. of water, precipitate with 10% Neutral Lead Acetate Solution (about 3 Cc.), adding a little Kieselguhr. Allow to stand for a  $\frac{1}{2}$  hour, filter off on the pump, wash the precipitate slightly. Remove excess of lead from the filtrate with 10% Sodium Phosphate Solution (about 2 Cc. required) and filter. Add a little Calcium Carbonate (about 0.2 Gm.) to the filtrate (to prevent possible hydrolysis of the glucosides), and evaporate to dryness on a water-bath. Add about 2 Gm. of dry washed sand to the residue and extract with Chloroform five times by thorough trituration, using about 10 Cc. on each occasion. Filter and evaporate the Chloroformic Solution and extract the residue with warm water on the water-bath, using 10 Cc. and 5 Cc. and again employing sand. Filter, evaporate to dryness in a porcelain basin, extract the residue again with cold Chloroform to purify it (about three or four quantities of 5 Cc. each, using dry sand and triturating thoroughly with a small pestle) and filter. Evaporate the combined Chloroformic Liquors and dissolve the residue in 4 Cc. of Glacial Acetic Acid. Mix 0.1 Cc. of this Acetic Solution with 1 Cc. of Sulphuric Ammonium Molybdate Reagent in a 5×1 Cm. test tube and compare the depth of colour after five minutes with the scale below—this coloration indicates the *content of combined "active water soluble" Glucosides* (probably including Digitoxin). Further, if 0.1 Cc. of the Acetic Solution be mixed with 0.5 Cc. of Glacial Acetic Acid, and this be layered upon 1 Cc. of the Sulphuric Ammonium Molybdate Reagent, the typical blue ring showing presence of Digitoxin should be formed.

### SCALE.

BELOW  
STANDARD.  
No. 0.

STANDARD.

No. 1.

ABOVE STANDARD.

No. 2.

No. 3.



= M.L.D. of 0.9 Cc.

= 0.75 Cc.

= 0.6 to 0.5 Cc.

= 0.4 to 0.3 Cc.

Mount the tubes on a little slab of Plasticine and observe the colours by direct transmitted light using a white background.



By means of this test results closely approximating the physiological "M.L.D." results were obtained with the samples of Tinctures referred to.

The conclusions of the investigation were as follows:—

(1) Digitalis preparations can be assayed by a simple colorimetric chemical method.

(2) The process, though not claiming absolute accuracy or comparison with the physiological methods, will, at any rate, show whether a tincture is *above* or *below standard*, and it will with certainty show an excessively strong or a weak preparation. The method uses only a small amount of tincture. The apparatus and reagents are perfectly simple, and such as a pharmacist would have at hand. Weighing of residues of questionable purity by means of an accurate balance is not introduced. The process takes about three hours to carry out. (Several specimens can be operated upon at once without taking very much longer time.)

(3) There are strong indications that digitoxin is not entirely insoluble in water.

(4) The routine use of animals in assays is not justifiable if a chemical method can be devised to produce equivalent results. Their use in experiments in research work, is an entirely different matter. Furthermore, the pharmacist should, if possible, be able to assay all the drugs he dispenses.

(5) Selected leaves recently dried, as a general rule, will produce tinctures up to standard, but there is obvious danger in the variation which may occur. At present a patient might easily obtain a preparation twice as strong at one pharmacy as at another. Considering the fact that, with digitalis, prolonged administration in the treatment of heart affections is almost always necessary, and that the initial doses of digitalis are invariably large, it is evident that standardisation of its preparations is of great importance.

(6) Tinctures of commerce vary considerably.

In the original paper the author admitted that a tincture becoming weak physiologically might possibly still give the same colour test as originally. To settle this question a supply of **a tincture twelve years old** was examined by the process at the end of 1912, using a strong tincture "J" (*c.f.* Table) and a weak tincture of commerce as controls. This old tincture gave a colour reaction almost equal to "J." The three tinctures in question (under distinguishing marks) were simultaneously examined by a physiologist,—the combined results being as follows:—

	Dose per 100 Gm. frog.		W. H. Martindale's Colour Scale.
	Killed (M.L.D.)	Failed to Kill.	
Tincture "J".....	0·6 Cc.	0·5 Cc.	Strong = 3.
Tincture 12 years old .....	0·7 Cc.	0·6 Cc.	Strong = 2 to 3.
Weak Tincture of Commerce .....	0·9 Cc.	0·8 Cc.	Below Stand'd.

These results showed **the value of the process even with an exceedingly old tincture**—the fact that a tincture 12 years old should show activity at all would have been generally discredited.—L.i./13,77.

**Subsequent to this it was decided to store the entire series of Tinctures for one year and re-examine both chemically and physiologically.** This provided useful information (1) on the utility of the Test; (2) as to the generally acknowledged diminution in strength of Digitalis Tinctures.

The results obtained are given in the following table:—

**Results of a Comparison of Physiological and Chemical Standardisation of Digitalis Tinctures in Oct.—Nov., 1912, and after 12 months' storage, i.e., Oct.—Nov., 1913.**

Original M'rks.	1912.		1913. Stored by Author.		1913. Stored by Physiologist.	
	Colour and M.L.D.= Cc. per 100 Gm. frog.	Phys. M.L.D. =Cc. per 100 Gm. frog.	Colour and M.L.D. Marks known by Author.	Phys. M.L.D.= Cc. per 100 Gm. frog. Marks unknown by Phy- siologist.	Colour and M.L.D. Marks unknown by Author.	Phys. M.L.D. Marks known by Phy- siologist.
	1.	2.	3.	4.	5.	6.
A. ..	—	0.5	—	—	—	—
B. {	No. 2. 0.5 to 0.6	0.4 to 0.6	No. 2. 0.5 to 0.6	0.6 to 0.6	No. 1 (twice). 0.75	0.8 to 1.0
C. {	No. 2-3. 0.4 to 0.5	0.4 to 0.5	No. 2. 0.5 to 0.6	0.8 to 1.0	No. 1. 0.7	1.0 to 1.2
D. {	No. 2. 0.5 to 0.6	0.5 to 0.6	—	—	—	0.6 to 0.8
E. {	No. 1-2. 0.6 to 0.7	0.6 to 0.7	—	—	—	1.0 to 1.0
F. {	No. 2. 0.5 to 0.6	0.5 to 0.6	No. 1. 0.75	1.0 to 1.2	No. 1-2 (twice). 0.65	0.8 to 1.0
G. {	No. 2. 0.5 to 0.6	—	No. 1. 0.75	1.0 to 1.2	—	—
H. {	No. 2. 0.5 to 0.6	0.5 to 0.6	No. 2. 0.5 to 0.6	1.0 to 1.2	—	0.8 to 1.0
I. {	No. 2-3. 0.4 to 0.5	0.4 to 0.5	No. 1. 0.75	1.0 to 1.2	No. 1-2. 0.65	1.0 to 1.2
J. {	No. 3. 0.3 to 0.4	1st. 0.3 to 0.4	No. 3. 0.3 to 0.4	0.8 to 0.8	No. 1-2 (twice). 0.65	0.7 to 0.8
	—	2nd. 0.5 to 0.6	—	—	—	—
K. {	No. 1. 0.75	0.6 to 0.75	No. 1-2. 0.6 to 0.75	1.0 to 1.2	No. 2. 0.65	1.1 to 1.2
L. {	Below Standard 0.9	0.3 to 0.4	Much below Std	0.6 to 0.8	—	0.8 to 1.0

The blanks indicate lack of material.



**Storage Experiments.—Continued.**

Original M'rks.	1912.		1913. Stored by Author.		1913. Stored by Physiologist.	
	Colour and M.L.D. = Cc. per 100 Gm. frog.	Phys. M.L.D. =Cc. per 100 Gm. frog.	Colour and M.L.D. Marks known by Author.	Phys. M.L.D. = Cc. per 100 Gm. frog. Marks unknown by Physiologist.	Colour and M.L.D. Marks unknown by Author.	Phys. M.L.D. Marks known by Physiologist.
	1.	2.	3.	4.	5.	6.
M.	No. 2. 0.5 to 0.6	1st. 0.8 to 0.81	No. 2. 0.5 to 0.6	1.0 to 1.2	No. 2. 0.6	1st. 1.0 to 1.2
	—	2nd. 0.5 to 0.6	—	—	—	2nd. 0.9 to 1.0
N.	—	—	No. 2. 0.5 to 0.6	0.6 to 0.6	—	—
O.	No. 2. 0.5 to 0.6	0.57 to 0.6	No. 1-2. 0.6 to 0.75	1.2 to 1.4	No. 1 (twice). 0.75	1.2 to 1.3
P.	Below Standard. 0.9	0.8 to 0.9	No. 1-2. 0.6 to 0.75	1.2 to 1.2	Below Standard. 0.9	1.4 to 1.4
Q.	No. 3. 0.3 to 0.4	0.36 to 0.4	0.75	0.6 to 0.8	—	0.6 to 0.8
R.	No. 2. 0.5 to 0.6	—	No. 2-3. 0.4 to 0.5	0.8 to 1.0	—	—
S.	No. 2. 0.5 to 0.6	—	No. 1-2. 0.6 to 0.70	0.6 to 0.8	—	—
T.	No. 2-3. 0.4 to 0.5	0.4 to 0.5	No. 2-3. 0.4 to 0.5	0.8 to 1.0	No. 2-3. 0.5	1.0 to 1.2
U.	—	0.2 to 0.3	No. 1-2. 0.6 to 0.7	0.6 to 0.8	No. 1. 0.75	0.6 to 0.8
V.	—	—	No. 2. 0.5 to 0.6	—	No. 1-2. 0.65	0.9 to 1.0
W.	No. 2-3. 0.4 to 0.5	0.6 to 0.7	No. 3. 0.3 to 0.4	0.6 to 0.8	—	0.9 to 0.9

Comparing the Chemical (Colour Scale) Results in columns 1, 3 and 5, it will be seen that we show a distinct falling off in strength after keeping one year in practically all the Tinctures.

Our physiologist's results (columns 2, 4 and 6) are similar. He shows falling off in all the Tinctures. His results indicate a more marked general diminution in strength than the colour figures.\* (NOTE.—Other workers have found a Tincture to decrease in strength by physiological test about 10% only in a year. Many workers in the past have stated that Digitalis Tincture is not so unstable as is supposed. Haynes, as also Hatcher and Eggleston, quite recently showed that the diminution in strength is quite small.—*Vide* Vol. I., p. 346.

\* See footnote on page 56.

There are clearly some discrepancies both in the chemical and the physiological results which are attributable to methods of storage and the laborious nature of the investigation. So far as the physiological data are concerned, these were all obtained upon Tinctures *undiluted*, whilst the Colour Scale data (col. 5) were in several instances obtained with Tinctures which had been diluted without our knowledge (1 to 10, 1 to 20, etc.) as our physiologist had run short of material to send back to us. Even this did not "trip up" the quantitative delicacy of the Colour Test, though the amounts of glucosides under investigation are exceedingly minute.

It will be seen that comparing columns 3 and 5 (in the one case knowing the marks and in the other not knowing them) the results are remarkably concordant. Owing to lack of material, our physiologist, again without our knowledge, *duplicated* several samples (A, F, J, O), and in these we obtained identical results on each occasion.

With regard to the fact that the physiological results show a more marked falling off in strength than our colours indicate, there is, of course, the well-known "frog variation" to consider. The frogs in the re-examination in 1913 were probably of a more vigorous strain than those used in 1912. It was hardly to be expected that a tincture 'W' found to be active physiologically after 12 years (M.L.D. 0.6 to 0.7 Cc.), should during the *next year* drop off, making M.L.D. 0.6 to 0.8 or 0.9.

To act as a check on the physiological results, we handed over to the physiologist in the middle of November, 1913, under marks "I" and "II" the following with a request for a final report:—

I. The 12 (now 13-year) old Tincture diluted to half strength\* with 60% Alcohol.

II. Tincture "N," These two were selected as respectively tinctures upon which we differed and agreed in the October, 1913, examinations.

The position was at that time (Oct., 1913), as follows:—

	Mark not known by Phys.	Mark known by Phys.
The 12-year-old Tincture (W) = { Colour No. 3.		
Tincture (N) =	0.3 to 0.4 Cc.	0.6 to 0.8 Cc.
	0.5 to 0.6 Cc.	0.6 Cc.
The new report was No. I. =	1.0 M.L.D. and No. II. =	0.6, i.e.,
Tincture (W) =	$\frac{1.0}{2}$	= 0.5 Cc. as M.L.D.
Tincture (N) =	0.6 Cc.	as M.L.D.

\* W. L. Symes, in an investigation on the activity and stability of digitalis tinctures, found that: (1) weak ones showed little or no change in a year or more; (2) those within 25% of standard were all more than 25% below standard after a year; (3) of those more than 25% above standard, only half were within 25% of standard after one year, these having lost 20 to 70% of their original activity. He found that of the tinctures he examined

20% had an initial activity of 0.6 to 1.0 (activity =  $\frac{\text{Standard M.L.D.}}{\text{Observed M.L.D.}}$  =

$\frac{0.75}{x}$ ) 22%, 1.1 to 1.25; 33% 1.4 to 1.7; 25% 1.9 to 2.5.—B.M.J. i./14, 1343

—W. H. Martindale in reply.—B.M.J. ii./14, 47.

W. L. Symes, P.J. ii./14, Aug. 1, has a further paper on this subject. In conjunction with Messrs. Stafford, Allen and Sons, he deals with the effects of climate on the plant. The weather factor, he says, may influence metabolism of the living plant. We fully agree that the plants "may 'yield' better in partial shade"—i.e., *weight* of leaf, but this does not entail extra yield of glucosides and even Dr. Symes' own table (III.) intending to upset our theory, that the most potent leaf (2nd year's) is collected after a *period of bright sunshine*,—in reality supports our view. e.g., the 1910-1911 leaf, the most active of the three, though growing in "Moist dull variable warm" weather in 1910 was collected in 1911 after "*dry bright hot weather*."

The number of hours of sunshine in 1911 in the 2nd and 3rd quarters, viz., 245, yielded him an 'activity' 2.1, whilst the next year, 164 hours, yielded 'activity' 1.3 to 1.4. Arithmetic—would indicate—if our theory is correct, 1.405! N.B.—Do not confuse this new 'activity' with M.L.D. s.





Frogs seem to have more power of resistance in the months of August and September. Though one may compare the pharmacological action of Digitalis with that of a chemically well-defined body, the action of Digitalis on the human organism cannot be estimated by such relationships, as this can only be effected by observations on patients. Schmiedeberg therefore proposed that all the Digitalis issued for medicinal use in Germany should first be standardised in a central Institute, and the crop of each succeeding year standardised to correspond exactly to the basis established in the first year.—L. ii./10,960.

Physiological standardisation of cardiac stimulants and depressants.—Am. Jl. Ph., Oct. 1910, 453.

Variation in the susceptibility of the guinea pig to the heart tonic group.—Am. Jl. Ph., Jan., 1912, p. 14.

“Heart Tonic Units.”—For this mode of standardisation advised by Houghton, “Extra Pharmacopœia,” XV., p. 343.

Squill, digitalis and strophanthus have strengths in proportion as 3 : 2½ : 1.—P.J. ii./05,754.

Comparison of Physiological Standards.—The various workers on the subject—Cushny, Dixon, Houghton, Martin, etc., have from time to time set up the most divergent time limits for the death of the frog employed in the test. We went very fully into this matter in the last Edition to which (Vol. I., p. 344) we must refer readers. **The customary method is to take the death of the frog in six hours** as the limit, but it differs with different workers.

A. D. Waller (Proceedings Phys. Soc. Dec. 19/08, Jl. Phys. Soc. vol. xxxviii.) examined the action of Digitalins on striated muscle. The **Muscle Test** is suitable for drugs soluble in Normal Saline, but for certain insoluble “Digitalins” it gives no direct information. Soluble Digitalins give effects closely similar to those obtained with Saponin—in particular was this the case with Digitalinum pulv. pur. Germanic.

Experiments with a tincture and infusion of Digitalis (*Off.*), the former diluted 20 times so as to bring the Alcohol down to 3%, which is necessary for the test, gave for this an effect to all appearances analogous with the full tonic effect on the heart—contraction of the muscle in the course of 15 minutes. The infusion produced little or no effect.

Of five “Digitalins” tried three were active, one being Digitalinum purum pulv. Germanic.

Digitalin, Merck (= Digitonin) was also one of the “active” preparations on striated muscle identical in action with Saponin. There is a general parallelism between physiological activity measured by response of muscle and toxic or narcotic power found by “killing power” per weight of living animal, the muscle method gives more precise results than the latter.

The method is applicable to physiological standardisation of Digitalis and allied preparations.

A. J. Clark finds (contrary to Waller) that the Digitalis group, which produces systole of the frog's heart, has little or no action on striped muscle, but that the Saponins in Digitalis which have little action on the heart will readily produce rigor in the frog's striped muscle. The action of Digitalis preparations on striped muscle depends on the quantity of Saponin and bears no necessary relation to the activity of the drug as affecting the heart.—L. ii./12,460.

Pithing frogs prior to experiment is as follows:—The brain of the animal is destroyed from the nape of the neck upwards, *i.e.*, the spinal cord is divided in the neck and then a wooden pointer is passed up into the brain (the centres of feeling), thus leaving the spinal cord intact and the heart untouched. A frog has been known to “live” for years with its brain destroyed. The animal feels nothing but its heart goes on beating and its reflex centres are alive.—Gordon Sharp, P.J. i./13,21.

### *References to work on Physiological Standardisation.*

L. ii./08,408, Leaderette on Crawford's work ex Am. Jl. Ph., July, '08; L. i./09,1744; L. ii./09,1174; P.J. ii./09,473,504; Martin, P.J. ii./09,149.

Experiments in America show that the drug can be standardised and lethal dose determined by injecting the drug into the femoral vein of a cat along with Ouabain, the toxicity of which is said to be constant.—C.D. i./11,738; see also Jl. Am. Med. Ass. 1911. vol. 56, p. 1198;



A RÉSUMÉ OF THE VARIOUS PHYSIOLOGICAL METHODS FOR STANDARDISATION OF DIGITALIS SUGGESTED HITHERTO.—Guinea-pigs possess no advantage over frogs for experiments. Lethal dose methods are unsatisfactory. The fact that a preparation kills an animal is no proof of the therapeutic value. Frog heart methods (Focke's and the 1 hour) are not lethal dose methods, and they are accurate within 10%.—Am. Jl. Ph., '11, p. 201.

**Digitalis Flowers**, S. Hirohashi, Pharm. Soc. of Japan Journal, No. 369 (per C.D.), states the Digitalis flowers probably contain more active principles than the leaves (? W. H. M.). He found that an absolute alcohol extract of flowers fourteen months old was stronger physiologically than a similar preparation of fresh leaves. So far as the activity of the fruit is concerned, he puts it at the same as the leaves, while the leaf-stalk is not so active as the leaves.

**Digitalis Seeds** are said to be ten times more toxic than the leaves. Tincture suggested.—P.J. ii./11,231.

The seeds contain very little Digitoxin, which is generally considered the most valuable constituent and a relatively large amount of Digitonin which has little or no use as a cardiac tonic.—Dixon, Q. Jl. Med. Jan. '12,297.

We prepared a **Tincture of the Seeds**. Our physiologist reported as follows upon it. Tested on the excised frog's heart, it was found that after removal of the Digitonin in which it was rich, the seed preparation proved to be weaker than an ordinary Tincture. Hence as it seems to be therapeutically weaker and yet more toxic than Leaf Tincture, it does not appear to be a desirable preparation. Digitonin is considered to be irritant to the alimentary canal.

### *General References :—*

The decomposition products of the glucosides in the drug may of themselves be valuable. The best preparations of Digitalis are those made without intervention of reagents.—P.J. ii./13,573.

H. Deane finds the physiological test not always correct; for example, a fat-free tincture proved stronger than the ordinary tincture. It had been found that the autumn leaves gathered after a wet summer were about the same as the previous year's (relatively dry) crop, while leaves gathered before the wet weather were weaker in glucosides.

The ash of the leaves contains Manganese.—Burman Schweiz. Woch., 1911,562.

### **Pharmacology of Digitalis.**

On the one hand it exercises a direct effect on cardiac muscle, while it also heightens the vagus inhibition of the heart. By the use of Atropine it was found possible to cut out this second effect, and thus to study the direct cardiac action.—L. ii./12,1668.

## **TABLE OF THE COMMON ENZYMES AND FERMENTS.**

ENZYME OR FERMENT.	SOURCE.	ACTION.
<b>Amylopsin or Diastase</b>	Malt and pancreas.	Converts starch into dextrin and finally maltose, <i>c.f.</i> , Vol. I. pp. 502, 585. <i>Vide</i> also Farr p. 61.
<b>Amylase</b> ..	Human and cow's milk and in human saliva	Hydrolyses starch as far as dextrin.—B.M.J. i./13,1067.
<b>Calotropis Procera</b>	Latex of.	Contains an enzyme, <i>q.v.</i>
<b>Catalase (see also Peroxidase)</b>	Blood and body fluids, <i>e.g.</i> , milk	Decomposes Hydrogen Peroxide.—B.M.J. i./13,1067.
<b>Cellulase</b> ..	Grass eating animals	Converts cellulose into sugar, as in the case of gramini-voracious feeders.—L. i./13,470.
<b>Chymosin, see Rennin</b>		

ENZYME OF FERMENT.	SOURCE.	ACTION.
Digestin ..	Okazaki Fungus.	Converts starch into sugar and peptonises milk, <i>c.f.</i> , p. 505.
Emulsin ..	Almonds.	Hydrolyses glucosides, <i>e.g.</i> , Amygdalin, <i>vide infra</i> , also Vol. I., p. 131.
Erepsin ..	Cauliflowers.	Acts as a tryptic ferment.—C.D. ii./13,851.
Fibrin Ferment	Blood.	Forms the clot when blood is shed, p. 230.
Hydrogen Peroxide and Ferrous Sulphate in certain proportion	—	Liquefy starch.—C.D. ii./13 851.
Invertase ..	Intestinal juice and produced by yeasts	Is capable of converting 200,000 times its own weight of cane sugar into invert sugar.—C.D. ii./13,851.
Lactase ..	Animal body.	Converts lactose into galactose.—L. i./13,470.
Lactic Acid Ferment	Milk.	Converts lactose into Lactic Acid.
Lipase ..	Pancreatic juice, blood plasma and many plants.	Converts fat into fatty acids and alcohol.—L. i./13,470.
Myrosin ..	Mustard seeds.	Hydrolyses the mustard glucoside, Vol. I., p. 718.
Oxidases ..	Tissues, especially Columnar Epithelium & glandular.	Oxidise purins, alcohol, aldehyde, phenol and tyrosin.—L. i./13,470.
Papain ..	The juice of <i>Carica Papaya</i> .	} Convert Albumin into Peptone in acid solution, pp. 590, 600.
Pepsin	Stomach, <i>e.g.</i> , Pigs.	
Peroxidases and Catalases	Blood and body fluids, <i>e.g.</i> , milk.	Oxidizing agent.—B.M.J. i./13, 1067. Set free Oxygen from Hydrogen Peroxide.—L. i./13,470. The action of these bodies is analogous to that of the Colloidal metals, or they may depend on presence of latter.
Perhydridase ..	Ditto.	Reducing agent.—B.M.J. i./13, 1067.
Ptyalin ..	Saliva of the mouth	Converts starch into sugar,
Rennin or Chymosin	Stomach of sucking animals, <i>e.g.</i> , calf	Coagulates the casein in milk, effecting clotting.—L. i./13, 470. <i>c.f.</i> , Vol. I., p. 600.
Steapsin, Piolyn or Lipolytic Ferment	Pancreas.	Decomposes fats into glycerin and fatty acid, Vol. I., p. 585.
Thrombin ..	Blood.	Coagulates fibrinogen into fibrin.—L. i./13,470.
Trypsin ..	Pancreas.	Converts albumin into peptones in presence of dilute alkali, Vol. I., p. 585.
Urease ..	Urine, especially in catarrh of bladder	Converts urea into Carbon Dioxide and Ammonia.—L. i./13,470.
Zymase ..	Yeast.	Converts sugars into alcohol, Vol. I., p. 253.



**Coenzymes or Activators** accelerate the action of enzymes, *e.g.*, *Enterokinase*, the constituent of the intestinal fluid which activates tryptase or trypsin.—L.i./13,470.

Ferments and Fermentation.—Na. July, 1911, p. 4.

E. H. Farr, in his Pres. Add. B.P. Conf., 1914, gave an interesting account of enzymes of which he states 120 are known. He pointed out the methods of stabilisation that are used in France for herbs and at the same time indicated that our methods should not be hastily altered seeing that our drugs have gained repute on non-stabilised material.

In some cases several enzymes may take part in the hydrolysis of a glucoside. With the complex **emulsin**, for instance, the hydrolysis of amygdalin takes place in three stages:

1. Amygdalase resolves amygdalin into amygdalic nitrile glucoside and one molecule of glucose.

2. Beta-glucosidase hydrolyses the amygdalic nitrile glucoside into amygdalic nitrile and glucose.

3. *d*-Oxynitrilase decomposes the amygdalic nitrile into benzaldehyde and HCN.

Side chain theory in enzyme action.—E. S. Edie, B.M.J. ii./14,506.

## ERGOTA.

*In Vol. I. we deal fully with the active principles of Ergot, to wit, the Alkaloid Ergotoxine and the co-existing Amines to which reference is to be made.*

Ergot was found to become 7 or 8 times weaker after being kept one year, whilst aqueous extracts of Ergot begin to lose activity in a few hours.—L. ii./o8,408.

Kraemer thinks Ergot might possibly be cultivated on nutrient media made from cereals such as wheat and rye.

It was found that not only were fluid extracts physiologically active in proportion with the amount of precipitate they yielded on dilution with water, but also in proportion as this precipitate yielded high percentage of Benzol extractive. Benzol, however, does not exhaust the drug completely. The Benzol extractive is a yellow resin, soluble also in Alcohol, insoluble in Acids, but readily soluble in solutions of the Hydroxides. Other characters go to deduce that the body is the Sphacelotoxin of Jacobi.—Am. Jl. Ph.—May '09, 215.

Yield of alkaloid 0.06 to 0.12%.—P.J. ii./o4,475; P.J. ii./o5,580.

No chemical assay method recognised. White Cross Society wanted 0.1% Alkaloid.—C.D. ii./o9,597.

Samples yielding high extractive to water inferior therapeutically to ones yielding low.—Southall's Lab. Rep., 1907. Nine samples gave from 14.56 to 20.57%.—average 16.7% water-soluble *ibid.*—1912.

Spanish Ergot is better than Russian.—Martin. (This is our opinion also.) In physiological assay uterine muscle contraction is the only true test.—P.J. ii./90,149,211.

⑤ **Ergoxanthin**, a principle found in ergot. A brief historical summary of the discovery of the alkaloids of ergot.—Am. Jl. Ph., Sept. 1910,410.

## EUCALYPTI OLEUM.

**Eucalyptol.** *Syn.* Cineol, Estimation of.

The Phosphoric Acid Method may be used as *Off* in Oleum Eucalypti. It is more accurate than the Resorcinol method—the latter gives results far too high. The U.S. process gives results too low.

Dodge suggests destroying the Terpenes with cold 5% Potassium Permanganate Solution and after 24 hours contact dissolving the Manganese Dioxide with Sulphuric Acid and measuring the volume of unoxidised Eucalyptol. C. T. Bennett finds the method works with Oils rich in Cineol, but not with low grade Amygdalina Oil.—P.R. 1912, 276,295.

If 2 Cc. be mixed with 4 Cc. of glacial acetic acid and 3 Cc. of Saturated Aqueous Sodium Nitrite, when gently stirred should not form crystals of Phellandrene Nitrite (exclusion of oils containing much phellandrene)—U.S.

*Off.* has this test modified by addition of Petroleum Spirit.

The Australian Oils with high Eucalyptol Content are less desirable pharmaceutically on account of the irritating Aldehyde which produces coughing.—P.J. ii./10,437. In a paper on Antiseptic Power of Essential Oils (*c.f.*, p. 101), we wrote:—

‘As the action of Eucalyptus Oils is generally considered due to antiseptic power, it would seem desirable not to exclude oils rich in Phellandrene.’ We also recommend that the Oil must not be of such a character as to produce a choking sensation on inhalation. This spasmodic effect is stated to be produced by aromadendral and other Aldehydes. Of three samples—Eucalyptol, Oil of Eucalyptus Globulus, and Oil of Eucalyptus Amygdalina—under discussion, the ‘Amygdalina’ produced by far the most choking, and the ‘Globulus’ had by far the pleasantest smell.

Amygdalina Oil was deofficialised because it was supposed that the efficacy of Eucalyptus Oil is due to Eucalyptol; but it was pointed out in 1885 that the reputation of the Oil in Europe was based upon the use of Amygdalina Oil.—C. D., Dec. 3, 1910.

**Phellandrene**,  $C_{10}H_{16}=135.128$  I. Wts. is a large constituent of the oil of *E. Amygdalina*. The irritating effect of some oils when inhaled has been attributed to this body, but the more general view is that the Aldehydes produce it.

When Phellandrene is detected in Eucalyptus Oils this is evidence that Amygdalina Oils are present.

The oil distilled in Victoria can be divided from the Chemical standpoint into four classes.

	Eucalyptol content.	O.R.	Phellandrene.	Soluble in 70% Alcohol.
(1) Mallee Oils ..	76%	0°	Absent	1½ vol.
(2) Globulus Oils ..	60%	0°	Absent	1½ „
(3) Gippsland Oils ..	30%	–20°	trace	1¾ „
(4) Amygdalina Oils ..	—	–50°	present	insol.

—C.D. i./13,504

Parry reports (C.D. i./13,358) the practice of diluting B.P. Oils with *Amygdalina* Oils so as to come just within official limits. This should be stopped. We agree with him that if it is permissible it would be quite as legitimate to use Camphor Oil or Castor Oil or anything else for such ‘standardisation.’

Eucalyptus Oil (*Amygdalina* Var.) is used in metallurgy in treating refractory ores, which are ground with water to which a small percentage of the oil is added, the effect of the oil being to bring the mineral particles to the surface.—C.D. ii./10,50. Enormous quantities of the oil have been consumed in preparing sulphides of zinc and lead. About ½ lb. oil is emulsified by vigorous shaking with about 100 gallons of water, and with this mixture the moistened or powdered ore is stirred. The oil absorbs the sulphide particles and carries them to the surface, together with the gold and silver contained in them, up to 95 per cent. of the actual content of the powdered ore being recovered by the process. The Barrier mines already consume about 10 tons of eucalyptus oil monthly.—Schimel & Co.’s Report, per Austr. Jl. Ph., Dec. 1911. See also C.D. ii./10,679. “Phellandrene Oils” work better than others and can thus be used up.—Na., June 1911 584; P.J. ii./11,30.

West Australian Eucalypts and their Oils. **Aromadendral** is an aldehyde contained.—P.J. ii./95,356,382.

Transvaal Oil is of excellent quality.—P.J. i./09,4.

## FERRUM.

The element iron is tetravalent, but the Fe atom occurs in compounds, apparently either as di- or tri-valent—the explanation by some chemists is that there are present “double atoms” held together either by 2 or by 1 linkage. Iron salts may thus be either Ferrous, in which they are traceable to the oxide FeO, or Ferric, as in Fe<sub>2</sub>O<sub>3</sub> (ferric oxide or sesquioxide).

	Fe=		Fe≡
Ferrous		Ferric	
	Fe=		Fe≡



### Pilula Ferri (Off.).

A little Reduced Iron added would prevent oxidation.—P.J. ii./03,916.

The employment of sodium bicarbonate in place of sodium carbonate, together with plenty of water, a little honey and gum acacia, produces a pill which will keep unoxidised for a long time.—C.D. i./05,793; P.J. i./05,765.

The original formula was published in 1832:—Dried Ferrous Sulphate and dried Potassium Carbonate equal parts with Mucilage of Tragacanth and Powdered Licorice.—P.J. ii./06,369.

Iron acts more as a stimulant to the blood-forming organs than as a constituent of new blood. In whatever way it enters the blood corpuscle iron is an essential factor in treatment.—B.M.J. ii./09,1423.

In pernicious anæmia rapid increase in number of red corpuscles under Blaud Pill capsules.—B.M.J. i./09,209.

Patients suffering from chlorosis improve more rapidly under a ferrous carbonate preparation so far as hæmoglobin content is concerned, than under Iron-protein preparations.—P.J. ii./11,16.

### Blaud Pill Estimation.

The white or other coatings having been carefully removed the weight of two pills should be carefully noted. They are dissolved in a beaker in a small quantity of water, say 15 Cc. with sulphuric acid 5 Cc. Decinormal solution of potassium bichromate (4.87 Gm. in 1,000 Cc.) is then run in until a drop of the solution no longer gives a blue colour with drops of potassium ferricyanide solution arranged on a white tile. Multiply the number of Cc. of Bichromate solution used by 0.0115 to obtain the amount of ferrous carbonate in grammes in the two pills.

Composition of 30 samples of Blaud's Pill. Some samples appear to have been made from ferrous carbonate, some contained very little sodium carbonate whilst some contained potassium carbonate.—P.J. ii./11,320.

Blaud's Pills have ceased to be proprietary here though they are the subject of a patent on the Continent.—E. J. Parry, P.M.C.E., C.D. i./13,560.

### Ferri et Ammonii Citras Viridis.

To prepare a scale compound of ferric ammonium citrate of a green colour the proportion of acid should be raised to one molecule and a half of citric acid to one atom of ferric iron. Larger quantities of citric acid heighten the green colour, but the salt becomes more hygroscopic.—R. C. Cowley, C.D. i./11,315.

Some recent experiments by us on this matter show that the proportion of Ammonia is also of importance. Very light green scales can be produced by using only  $1\frac{1}{4}$  molecules of Citric Acid to 1 atom of "ic" Iron and  $1\frac{1}{2}$  molecules of  $\text{NH}_3$ . This yields a preparation containing 22%  $\text{Fe}_2\text{O}_3$ .

### Syrupus Ferri Iodidi (Off.).

The addition of Hypophosphorous Acid is objected to—it is the instability of Ferrous Iodide that makes it so valuable therapeutically. The absorption of the Iodine is required,—added preservative prevents or retards this. It is recommended to double the amount of iron in the U.S. preparation. Place Iron Wire 25 Gm. in a 500 Cc. flask and wash well with water, add Water 150 Cc. and then Iodine 41.5 Gm. Shake, and when the mixture is of greenish colour and free from Iodine odour boil for five minutes. Filter through a folded filter paper, the point of which dips below the requisite 700 Gm. of Syrup. When the liquid has run through wash the flask and filter with a mixture of Syrup and Water each 25 Cc., previously heated to boiling, finally make the weight 1,000 Gm.—P.J. ii./10,576.

Citric acid  $\frac{1}{2}\%$  is even better than hypophosphorous acid as preservative.—P.J., ii./09,405.

Ferro-Silicon.—A physico-chemical alloy of Iron and Silicon used in the manufacture of steel goods where easy working and high tensile strength is required, in contact with water or moist air gives off poisonous gas, i.e., Phos-phorettered Hydrogen, Arseniuretted Hydrogen *inter alia*, hence dangerous unless correctly used. That containing between 40 to 60% Silicon contains the most impurities.—L. ii./10,220.

### Syrupus Ferri Phosphatis Compositus.

Estimation of Iron and Calcium.—The estimations of Iron and Calcium in this preparation have to be conducted separately.

**Iron.**—Dilute 20 Cc. of the Syrup with water considerably, heat on a water bath, add Ammonia in slight excess and allow precipitate to deposit on the water bath. Collect and wash quickly with boiling water. Ignite and dissolve in Hydrochloric Acid, add Ammonia in slight excess, collect and wash slightly and dissolve in dilute Sulphuric Acid. Reduce by boiling with copper foil and titrate with Permanganate. The iron is expressed as Ferrous Phosphate.

**Calcium.**—Add about 1 to 2 Gm. of Citric Acid to 20 Cc. of Syrup and a little Hydrochloric Acid. Make slightly alkaline with Ammonia and finally just acid with Acetic Acid. Add Ammonium Oxalate in excess and estimate Calcium as usual.

Some commercial samples ranged from 0.13 to 0.5 grains per drachm of Ferrous Phosphate and Calcium Phosphate from 'a trace' of 0.9 grains per drachm.—Salamon and Seaber, C.D., July 5, '13.

## FILIX MAS,

### Extractum Filicis Liquidum (Off.).

Up to a certain period the greater part of the Male Fern Extract of commerce was adulterated with 30 to 60% Castor Oil. Sp. Gr. should not be below 1.0 (Off.) R.I. at 20° C., not below 1.5 usually 1.505 to 1.509. Must dissolve entirely in 10 volumes Petroleum Ether. Saponification value 230 to 250. Unsaponifiable matter 8 to 11%. Fatty acids should have mean combining weight of 240 to 255. Crude Filicin not less than 20%.—E. J. Parry, P.J. i./11,778.

**Estimation of Filicic Acid in Male Fern Extract.**—A series of genuine extracts contained between 19 and 26% of crude Filicic Acid, hence the standard of the P. Helv. (26 to 28%) is thought to be too high. A fair average value should be 22%, and a minimum 20%. The 3% Baryta Solution of the P. Helv., is best for estimating the acid which should be characterised. In sampling it is necessary to stir up well.

**Note.**—Poulson says the Extract contains Filicin in addition to Filicic Acid. The first is amorphous and is deemed active, the latter is inactive and crystalline and is viewed as the lactone of Filicic Acid. Kraft regards the two bodies as isomeric.—C. A. Hill, P.J. ii./13,126.

It would seem best, therefore, in carrying out the assay process of P. Helv. to term the extractive 'Crude Filicic Acid.'

E. F. Harrison examined a number of Commercial Extracts and differs from Parry's limit figures, notably in Crude Filicin content, which may fall below 20%.—P.J. ii./13,128. Off. requires not less than 20% Filicin by Barium Hydroxide method.

Most tæniacide drugs contain a phloroglucin group. Tschirch.—P.J. ii./09,421.

## GELSEMII RADIX (Off.).

A standard of 0.5% total alkaloids for the root, and 0.05% for the tincture has been suggested.

An assay process (in U.S.P.) should be provided as the drug varies.—Am. Jl. Ph., Feb. 08,77.

'Gelseminine' has been regarded as the soft resinous alkaloidal residue remaining after Gelsemine Hydrochloride has been crystallised from alcoholic solutions of the mixed alkaloids. Cushny regarded this as a powerful poison resembling Conine. L. E. Sayre has separated it into at least two distinct bodies having different solubilities and different reactions with Reagents. H. W. Emerson reports that Pharmacological examination showed: (1) that 'Gelsemine Hydrochloride' contrary to previous statements has an inherent power as a heart depressant preceded by a period of excitation,—this is not due to admixture of Gelseminine, (2) An alkaloid soluble in Ammonia which if found to be a separate alkaloid, may be called Gelsemoidine. It is a less powerful depressant than 'Gelsemium' (?). (3) 'Gelseminine' (insoluble in Ammonia) is less toxic than any other one of the poisonous principles. They all have paralysing effect in different degrees.—P.J. i./11,242



C. W. Moore provides a further paper in which he mentions having purified the 'Gelsemine' and obtained it with M.Pt.  $160^{\circ}$  of formula  $C_{20}H_{22}N_2O_2$  by crystallising from Acetone.—P.J. ii./10,584; C.D. ii./10,52; J.C.S.T. i./11, 1231.

N.B.—In both these last two papers the name 'Gelsemine' is apparently given to the alkaloid which we and others have for years past termed Gelseminine. Hence to understand the data in these two abstracts the transposition should be made.

L. E. Sayre contributes a further paper on this subject.—Jl. Am. Ph. Ass., May, 1912, P.J. ii./12,73, obtaining 6.4 Gm. "Gelseminine" (i.e., our amorphous alkaloid Gelsemine) and 0.44 Gm. "Gelsemine" Cryst. (i.e., our Gelseminine) from 50 lbs. of crude material. He suggests that the name **Sembervirine** should replace "Gelseminine" (i.e., Amorphous Gelsemine as we understand it). To us all this dispute over the naming of the body appears unnecessary—especially so late in the day.

**Identification of Gelsemium.**—It does not contain any Aesculin. The fluorescent body is Scopoletin (Aesculetin—5—Methyl Ether). If 0.5 Gm. of the ground drug be heated in a tube with Chloroform, the mixture filtered and the filtrate shaken with water to which a few drops of Dilute Ammonia have been added, the aqueous layer on separation shows distinct blue fluorescence,—indicating presence of Scopoletin.—F. Tutin, P.J. i./12,157.

## GLYCERINUM.

Glycerin occasionally crystallises. Such crystals melt at  $17^{\circ}$  C.

Fat decomposition and recovery of Glycerin.—Am. Jl. Ph., Feb., 1910,71.

Suggested U.S.P. tests for Glycerin.—Am. Jl. Ph., June, 1910,253.

**For the Estimation of Glycerin in Galenical Preparations**

(Naylor) consult—P.J. ii./09,131,139, B.C. D. ii./09,138, or Edition XIV..p. 329.

**Glyceryl Carbonates.**—Glycerin and Phenyl Carbonate react at moderately high temperatures in vacuo. The completely saturated product is a solid crystalline substance with m.pt.  $138^{\circ}$  C.—insoluble in water. Phosgene may also be used.—Patent 19,924 of 1911, vide P.J. ii./12,299.

Ultra violet rays from a powerful Mercury-quartz lamp decompose Glycerin with formation of Formaldehyde.—P.J. ii./12,7.

## Glycerinum Boracis.

It is thought that the bodies combine to form Glycerol-Boric Acid, a monobasic acid expressed by the formula  $HC_2H_5OHBO_3$ —this has however not been isolated.—P.J. i./11,90,104.

## Microscopic Glycerin Jelly.—

Dissolve Gelatin 12.5 in Water 100, add Glycerin 100 (warmed) clarify with egg albumen 12.5 and to the product add Salicylic Acid 1 in Alcohol 12.5. We find this formula to work satisfactorily.

## GLYCYRRHIZA. (Off.).

### Glycyrrhizinum Ammoniatum, U.S.

According to some views (c.f. P.J. i./11,258) 'Glycyrrhizin' now applies to the sweet substance found in liquorice root by Tschirch to be a mixture of Calcium and Potassium Glycyrrhizates and hence containing neither Ammonia nor Nitrogen. This mixture is colourless when pure, the yield being about 3%.—c.f. Y.B.P.—1907, p. 73.

Tschirch discovered that Glycyrrhizinic Acid is the Diaglycuronic Acid ester of Glycyrrhetic Acid. It has glucosidal properties. Glycuronic Acid, c.f. 172 is of importance in animal life—an unexpected fact, as the most varied sugars are at the disposal of a plant if it wishes to form Glucosides.—P.J. ii./09, 21; c.f. also Y.B.P., 1907,73.

Liquorice Juice of commerce contains 10 to 15% and more of Glycyrrhizin. White Cross Congress required only 6%. Umney.—C.D. ii./09,580. See so P.J. i./05,494; C.D. i./10,21.

**Analysis of Liquorice Juice.** A minimum of 9% of 'Glycyrrhizin' should be present in normally prepared edible juices—they should not contain more than 8% of sugars, reducing and non-reducing. In order to determine whether

the starch present (genuine juice may have starch present owing to crude method of filtration) be actual or added, the sample should be powdered, extracted with water and the residue taken up with 3% Ammonia Solution. The insoluble matter should never exceed 6%. Examine this under the microscope to trace source of starch, *i.e.*, whether added or of the same character as that in the root. The amount not dissolved in 70% alcohol should not exceed 16.5%. Gum should never be present in pure Liquorice Juice.—Parry, C.D. i./11,133.

Licorice Root and Extract. Method of examination. The resins are confined to the bark of the root. With 'mild' extraction with hot water they remain mostly in the marc.—Am. Jl. Ph., Dec., 1912.

Thirty-two samples of powdered liquorice examined. Three of the samples yielded less aqueous extract and nine exceeded the ash limit.—Professor H. G. Greenish and Dorothy J. Bartlett.—P.J. i./13,365,370.

*Off.* requires not less than 20% extract by Chloroform Water in the cold.

## GUAIACI RESINA.

The **PHYSIOLOGICAL ACTION OF GUAIACUM RESIN** is we believe not completely understood. The drug is acknowledged to have useful effect in gout and rheumatism.

In 1911-12 we conducted investigations to determine whether this Resin increases or decreases the elimination of Uric Acid from the human body. It was suggested (A. E. Garrod) that Guaiacum has a distinct effect in reducing the amount of Uric Acid excreted, *i.e.*, it was thought that the Uric Acid is eliminated in some other form, possibly Hippuric Acid.

A normal individual took Guaiacum Resin in 5 grain doses daily in the morning and the Uric Acid was estimated in the urines the same afternoon. Hippuric Acid was also estimated in specimens of the same urines by the method given by Allen, "Chemistry of Urine," p. 186. After a day's interval the Acids were estimated on several days without administration of the drug. The two series were then repeated on the same lines after an interval. Seeing that the diet of the individual could not well be controlled in weighed amounts of food as would strictly be necessary for an investigation of this kind, it was thought that to express the results in percentage Ratios of Uric Acid to excess of Solids (R.U.A.) over Water might yield more comparable results.

Joulie employs this method of indicating the constituents of Urine by Ratios *c.f.*, p. 246. Thus, taking a specimen of urine with the following 'Normal' factors in Gm. per litre.

Specific Gravity	1017.8	Cl.	..	..	..	6.865
Excess of Solids over Water	17.8	Urea	..	..	..	18.75
Physiological acidity in terms		Uric Acid	..	..	..	0.416
of $H_2SO_4$	0.849	Hippuric Acid	..	..	..	1.3
Total $P_2O_5$	2.083					(mean)

one may express the constituents as the following percentage ratios:—

Normal.

R.A.' Ratio of Physiological Acidity to excess of Solids over Water	4.77	( <i>i.e.</i> $\frac{0.849 \times 100}{17.8}$ )
R.P' Ratio of total $P_2O_5$ to excess of Solids over Water	11.17	
'R.U.' Ratio of Urea to excess of Solids over Water	100.53	
R.U.A.' Ratio of Uric Acid to excess of Solids over Water	2.33	
R.H.A.' Ratio of Hippuric Acid to excess of Solids over Water	7.3	
'R.P./R.A.' Ratio of Phosphoric Acid to ratio of Acidity (Joulie's factor)	2.45	

Ratio of Uric Acid, for example, is arrived at thus :  $\frac{0.416 \times 100}{17.8} = 2.33$



The results which we obtained are given in the the following table :—

**Effects of Guaiacum Resin on the Urine of a Normal Individual.**

	Date.	Sp.Gr.	Urea%	Uric Acid.	Hippuric Acid.	' R. ' U.A. '	' R. ' H.A. '
With Guaiacum	28/12/11	1·0207	2·29	0·09	0·09	4·43	4·34
" "	29/12/11	1·0247	1·29	0·08	0·1	3·34	4·04
" "	1/1/12	1·0215	2·56	0·105	0·15	4·88	6·97
" "	2/1/12	1·0241	2·82	0·10	0·2	4·2	8·29
Without Guaiacum	4/1/12	1·0229	2·42	0·06	0·1	2·62	4·36
" "	5/1/12	1·0249	2·42	0·08	0·2	3·16	8·03
" "	8/1/12	1·0255	3·09	0·10	0·225	4·11	8·82
With Guaiacum	11/1/12	1·0233	2·56	0·09	0·1	3·7	4·29
" "	12/1/12	1·0213	1·88	0·075	0·1	3·05	4·69
Without Guaiacum	24/1/12	1·0239	2·42	0·08	0·038	3·45	1·57
" "	25/1/12	1·0229	2·15	0·06	0·05	2·61	2·18

Average Uric Acid Ratio under Guaiacum Resin .. = 3·39

" " without " " " " " " = 3·19

" Hippuric Acid Ratio under Guaiacum Resin = 5·43

" " " " without " " " " = 4·99

The quantity of Hippuric Acid normally found is known to vary enormously *e.g.*, between 0·02 and 0·25%. From this we deduced for purpose of this investigation a mean normal R.H.A. of 7·3. A number of other investigations were conducted on analogous lines but need not be recorded.

One observes an average increase of Uric and Hippuric Acids during the ' + Guaiacum ' periods. It is not possible to draw a conclusion without further corroboration. The amount of each Acid from day to day is seen to be erratic, and the process of estimation of Hippuric Acid is not accurate. A. E. Garrod's opinion in the matter may yet be substantiated by further work. The publication of these data, even if erroneous, may perhaps induce someone in hospital practice, with facilities for keeping patients on exact diet, to enquire into the matter.

## HAMAMELIS.

### Liquor Hamamelidis.

A very considerable quantity of concentrated distillate injected into frogs and mammals produces no more effect than would be produced by similar amounts of distilled water. U.S.D.

U.S. employs dried bark ; the fresh leaves are not employed officially in U.S. though *Off.* the fresh leaves are directed for use in this country. This appears anomalous. The U.S. article in aroma and taste does not compare very favourably with Liquor Hamamelidis.—*Off.* (which cannot be made in this country). We have obtained a liquor comparing favourably with either by using the dried leaves.

Is chiefly prepared in the States of Massachusetts, Connecticut and New York from the small twigs preferably in the fall, when the leaves are off. From a ton of twigs 50 to 80 gallons of distillate is produced, to which 5 to 10% of alcohol is added to prevent change.

**Essential Oil of Witch Hazel.**—H. A. D. Jowett and F. L. Pyman have examined a specially-prepared sample, and find that its chief constituent is a sesquiterpene, other constituents being a phenolic substance, a mixture of fatty acids and a mixture of solid saturated hydrocarbons.—P.J. ii./13,129.

## HEXAMINA.

Experiments to determine which of the following :—*Hexamethylene tetramine itself*, *Formaldehyde set free therefrom in an acid urine*, or

even the Acid Sodium Phosphate alone used to increase the acidity of the urine.—is the active agent in overcoming bacilluria.

The amount of Formaldehyde passed in the urine by a patient taking a drug of this kind, even if split up, would be small compared with the volume of the urine.—*c.f.* p. 236.

A number of workers have recently set themselves the task of solving this somewhat complex problem. We classify their remarks below. We are fully aware that Hexamethylenetetramine is in itself non-bactericidal. We have recently substantiated that even a 10% Solution will not kill *B. Coli in vitro* (*c.f.* *Antiseptic Powers*, p. 197.). In this connection it should be added that the Salicylate (Vesalvine 'S') is more potent on *B. Coli*. It kills in 2½% Solution in 30 minutes. Now it should be noted that:—

(1) Hexamethylenetetramine is really a stable compound. It is only very slightly decomposed into Formaldehyde at body temperature. It needs *boiling* with mineral acid to decompose it to any extent.

(2) Our 1914 experiments show that 2% Formaldehyde (= 5% of Formalin) would have to be present in the bladder and other organs to promptly sterilise the urine! This quantity is never present in taking even a number of 10 grain doses of Hexamethylenetetramine.

We have recently again set ourselves to determine whether the effect of Hexamethylenetetramine is due to the small amount of Formaldehyde set free from it.

It is known that a patient with bacilluria and relatively low acid index (*e.g.*, 2° or less), taking hexamethylenetetramine alone fails to improve, but if Sodium Acid Phosphate be given simultaneously bacteria diminish as the degree of acidity rises. The high acidity, however, cannot be kept up for long, as it causes intense discomfort.

The following specimens of urine were, therefore, inoculated with *B. Coli* and loopfuls transferred to MacConkey's broth after 2½ minutes, 30 minutes and 3 hours contact, then the urines themselves were incubated and loopfuls transferred to MacConkey's after 18 hours incubation:—

(1) Urine alone with Acid Index = 0·7, as control.

(2) Urine with Sodium Acid Phosphate to make Acid Index = 6°.

(2a) " " " " " " " " = 3°.

(2b) " " " " " " " " = 1½°.

(3) Urine Acid Index 6° (No. 2 Urine) + Hexamethylenetetramine 0·13%.

(4) Urine Acid Index 0·7 (No. 1 Urine) + Hexamethylenetetramine 0·13%.

(This amount of Hexamethylenetetramine—0·13%—is such as would possibly be present in the bladder (1500 Cc. content) after 2 doses of 1 Gm.). *Not one inhibited the organisms with three hours contact. After 18 hours incubation* No. 3 urine was quite bright, all the rest showed strong growth. Inoculation of MacConkey's broth showed that No. 3 was sterile, all the rest giving growth. No. 3 gave a distinct reaction for Formaldehyde by Rimini's test, No. 4 gave none. This proves that although the proportion of Formaldehyde is (to our knowledge) insufficient to kill *B. Coli*, nevertheless, the small amount *slowly generated* from the Hexamethylenetetramine is sufficient *to inhibit growth* of the organisms and thereby to have a marked influence on bacilluria.—W. H. M., 1914 Experiments.



### *Results of Experiments by Others.*

Jordan by experiments on his own urine claims that the antiseptic power of Hexamethylenetetramine is directly concordant with the amount of Formaldehyde formed. He maintains, contrary to Cammidge, Cotyl and Salus (and ourselves) that a substance causing acidity of the urine (*e.g.*, Sodium Acid Phosphate) must be simultaneously given.—B.M.J. ii./13,651.

In Hexamethylenetetramine treatment give alkali to first neutralise poison of pure *B. Coli* infection and when symptoms subside give antiseptics in progressive doses. In agreement with Jordan, action of Urotropine depends on acidification of the urine and hence Formaldehyde production.—J. W. T. Walker, B.M.J. ii./13,654,657.

Further work also says therapeutic effect depends on the liberated Formaldehyde—this only occurs in truly acid body fluids. Hexamethylenetetramine is in itself not bactericidal.—B.M.J.E. i./14,28.

Infection of the Urinary Tract in Children by Coliform Organisms.—The usual treatment was (1) Alkalis, (2) Urinary Antiseptics, (3) local treatment of the bladder. None of them seemed of much value. The alkalis have been widely used with the idea that *B. Coli* does not thrive in an alkaline medium. This is not strictly true. It grows quite well in same but also grows well in an acid medium, while the usual pyogenetic organisms will not. The reason why the urine of these cases is acid is because *B. Coli* does not split up urea. Local treatment by washing out the bladder and injecting Iodoform seems to have good effect. Vaccines do good to the general condition but seldom remove pus from the urine.—W. M. Jeffreys, Q. Jl. Med., Apl., 1911, 267 *et seq.*

*B. Coli* thrive in Urotropinised urine (if alkaline).—Pr. 09,658.

## HYDRARGYRUM.

### Mercury, Detection of in Human Hair.

An amount corresponding to 1 in 90,000,000 can be found using 2 to 10 Gm. of the hair—in those who have undergone Mercurial treatment.

Free the specimen from grease by washing with ether, alcohol, and water, then digest in hydrochloric acid containing potassium permanganate. On complete solution treat with  $H_2S$ . Collect pp. and treat with Potassium Chlorate and Hydrochloric Acid. Filter and evaporate to small bulk. Boil gently a strip of copper foil in same. Dry the foil and place in a tube one end of which ends in a capillary. Exhaust and seal, then heat in a flame so as to sublime the mercury in the capillary. Globules may then be seen under the microscope.—L. ii./12,1737; P.J. i./13,31.

Volumetric Determination of Mercury.—Am. Jl. Ph. 1911, 311.

Mercuric Oxide is useful as a Volumetric Standard in Acidimetry and Alkalimetry and in Iodimetry, Oxidimetry and Argentometry. It is obtainable chemically pure. For method of proceeding in each case see Rosenthaler and Abelmann.—P.J. ii./13,144.

Iodides interact with Mercury and its salts forming Mercuric Iodide—this proved fatal in a child at Coventry receiving inunction of Ammoniated Mercury Ointment and simultaneously a solution of Iodine locally for ring-worm.—P.J. i./13,208.

### Hydrargyri et Potassii Iodidum.

#### (P) Mayer's Reagent.

Mercuric Chloride 13.546 grammes, Potassium Iodide 49.8 grammes, Distilled Water to 1 litre.

This reagent gives a precipitate with alkaloids.

Formerly methods of volumetric estimation of alkaloids by means of the above were in vogue, but the composition of the precipitates is variable.

### Unguentum Hydrargyri Nitratis.

Experiments by us at the end of 1909, with a view to determining the best mode of making this ointment, gave results which were summarised in our XIV. edition.

Martindale's Formula for Citrine Ointment.—Using only one-third of the *Off.* quantity of Acid and a volume of water equal to volume of Acid to dissolve the Mercury (in the cold), also employing White Vaseline in place

of the lard, and a temperature of  $87^{\circ}$  C. for mixing. Stir until cool and smooth. There was no effervescence. Even this reduced quantity of acid is more than theory demands for making Mercurous Nitrate (and slightly more than theory for Mercuric Nitrate), but excess of acid appears to be necessary for keeping qualities. Furthermore, the water we found was also desirable. This ointment examined three months after making was of good colour, smooth, and easily rubbed into the skin.

(NOTE.—*Off.* now maintains temperature  $90^{\circ}$  C. until frothing ceases)—the mixed lard and oil has initial temperature  $150^{\circ}$  C.

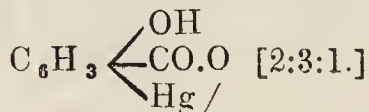
The principle on which the official ointment is made appears to be that the Nitric acid acting upon the mercury in the cold produces Mercurous Nitrate and Nitrous Acid, an excess of Nitric Acid being present. On adding to the fat the Nitrous Acid forms elaidin, and the heat of the fat causes oxidation of the mercurous salt with formation of more Nitrous Acid from the excess of Nitric Acid present. The excess of Nitrous Acid is driven off in the form of Oxides of Nitrogen.

Some discussion took place regarding the composition of this ointment. Cowley maintains that "it does not contain any nitrate of Mercury whatsoever." His statement is to the effect that Mercuric Nitrate is entirely decomposed in the presence of fats and that the product consists of "Mercuric compounds of Elaidic Acid and Acids produced by the oxidation of the fats."—C.D., Jan. 7, 1911.

We provided (C.D.i./11,63) the results of our experiments undertaken with a view to settling the matter. A separation process to define the exact form of the mercury is by no means easy to devise owing to the various complications present. A very large proportion of the Mercury is certainly present in a condition soluble in ether and in Petroleum Ether. We have since conducted a number of further experiments on the subject. Without describing same in detail we may say that our methods consisted (1) in finding the limit of solubility of Mercuric Nitrate in Petroleum Ether then determining the amount of Mercury in a Petroleum Ether solution of the Ointment using considerably less than the amount required for dissolving the  $\text{Hg}(\text{NO}_3)_2$ , possibly present. (2) Mixing  $\text{Hg}(\text{NO}_3)_2$  in proportion assumed in the Ointment with the fatty ingredients and then estimating, using Petroleum Ether as above. We are inclined to agree from this work that the Mercury is, in the main, not in the form of Mercuric Nitrate, but on the contrary at least 50% of it is in the condition of salts of fatty acids or their oxidation products, and that practically all the Nitric Acid is decomposed or dissipated by the process of manufacture. }

### Hydrargyri Salicylas,

P.G. terms the Compound Mercuric-Salicylic Acid and gives the formula



It will be seen that this indicates an entirely distinct composition from that usually assumed—the Mercury being linked direct to the Benzol ring. Schmidt, we notice, favours a compound of this formula—he draws attention to the slow precipitation of the mercury contained by Sulphuretted Hydrogen in support of the new view.

Patented Compounds with Hydrocyanic Acid, said to be valuable Antisyphilitics of mild action, and non-corrosive—suitable for subcutaneous injection.—P.J. ii./10,685.

### HYDRASTIS RHIZOMA.

**Assay Method.**—The drug in No. 60 powder is treated with ether, ammonia and water. A volume of the filtrate is shaken out with sulphuric acid and water. The acid solution is rendered alkaline with ammonia and shaken out with ether, the ethereal solution is evaporated and the residue weighed.

Rapid estimation method.—P.J. ii./05,580.

History of Hydrastis.—P.J. i./11,824.

There appears to be considerable loss in alkaloid in extracting the drug for Liquid Extract. Judging from Mann's figures—about 2% should be expected



in a well made extract.—P.J. i./09,366; C.D. i./09,426. This strength is now *Off.*

### Hydrastina (Alkaloid).

To distinguish from Hydrastinine:—A crystal dissolved in dilute sulphuric acid and 1 in 10 solution of potassium permanganate added, blue fluorescence develops. (U.S.)

### Hydrastinina.

*Synthetic Hydrastinine*, using piperonal as starting point. Piperonal known as heliotropin in the perfume industry, is cheaply made from safrol, the waste residues of the manufacture of camphor from camphor oil. Decker ("Zeitf. Angew. Chem.", 1911, 40); (*c.f.*, also Cotarnine).—C.D. ii./11,650.

## HYDROGENII PEROXIDI LIQUOR.

In the customary process of estimating the Volume of Oxygen produced in a Nitrometer with Permanganate and Sulphuric Acid it is better to use saturated magnesium sulphate solution rather than sodium chloride solution.

Copper Ammonium Sulphate Solution is now used instead of Permanganate and Acid.—*Off.*

Iodometric Determination.—Y.B.P. 1901,71.

P.G.V. gives method of estimating by titrating Iodine liberated from Potassium Iodide.

**Rapid Method of Estimating.**—Titrate 2 Cc. in presence of a little dilute Sulphuric Acid with a solution of Potassium Permanganate 5.06 Gm. per litre until decolourised. Each volume of this solution is equivalent to an equal volume of Oxygen. 1 Cc. of 10 volume  $H_2O_2$  decolourises 10 Cc. of the Permanganate, and 1 Cc. of 20 volume will decolourise 20 Cc. of it.—C.D. i./06,211. The explanation is:— $2KMnO_4 = 5$  atoms oxygen  $\therefore 316.06$  Gm. = 55.8 litres Oxygen, *i.e.*, 5.66 Gm. = 1 litre Oxygen,  $\therefore$  1 Cc. of the Permanganate Solution of this strength = 1 Cc. of Oxygen or 0.000287 Gm. approx.

Assay of Peroxide and amount of Acidity.—M. 1908; P.J. ii./08,460.

### Preservatives.

Benzoic Acid 0.05% added to Hydrogen Peroxide Solution is said to be a good preservative.

A little phosphoric acid is sometimes added as preservative. Acetanilide has also been employed and is said to be useful. It is thought to be first converted into anilin acetate, then oxidised to nitro-benzene, recognisable by the odour developed. (*v. infra*).

In the U.S.P. method of determination of free acid in Hydrogen Peroxide Solutions the presence of acetanilide appears to act the part of a free acid and to seriously interfere with securing accurate results. Direct titration in the cold gives sufficiently accurate results.—Am. Jl. Ph., Dec. 1910, p. 577; *v. also ibid.* Nov. 11, p. 519.

### Concentration of Hydrogen Peroxide.

Certain experiments.—Pharmacal Notes.—Sept., 1912, have shown that a 10 vol. Hydrogen Peroxide Solution (containing a little acetanilide as preservative) evaporated to half its bulk in a clean vessel at N.P. has approximately double its hydrogen Peroxide strength. The actual figures were:—

1000 Cc.	Actual Hydrogen Peroxide	3.04%.
450 "	" " " "	6.52%.
300 "	" " " "	9.89%.
200 "	" " " "	14.7%.
100 "	" " " "	25.2%.
50 "	" " " "	43.2%.

We have worked on this subject ourselves and do not find this substantiated except in the presence of Acetanilide in excess of the quantity commonly stated:—

1000 Cc. of 10 vol. Hydrogen Peroxide *sine* Acetanilide had strength 3% Hydrogen Peroxide. Evaporated to 300 Cc. the strength was 4.8%.

1000 Cc. with 1/100 grain Acetanilide to the ounce of Solution, evaporated to 300 Cc. showed a slight increase in strength. Evaporated further, *i.e.*, to 126 Cc. there was a marked loss of Hydrogen Peroxide not an increase,

1000 Cc. with 1/100 grain Acetanilide **to the ounce of actual Hydrogen Peroxide, i.e.,  $\frac{1}{3}$  grain approx. of Acetanilide per ounce of  $H_2O_2$  Solution,**—

Evaporated to 500 Cc., showed strength 6% Hydrogen Peroxide Solution.

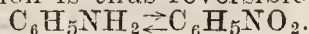
Evaporated to 300 Cc. showed strength 9% Hydrogen Peroxide Solution.

Evaporated to 120 Cc. showed strength 17% Hydrogen Peroxide Solution.

The same author repeats (P.J. i./14,536)—as a preservative 1/100 grain of Acetanilide to each fluid ounce is 'usually employed.'

We think '**per ounce of Hydrogen Peroxide**' is intended, at any rate this is the case in our evaporation experiments.

With regard to the Acetanilide *first undergoing hydrolysis to form anilin and acetic acid, and the anilin then being oxidised to nitrobenzene*, it is possible that at this stage the nitrobenzene undergoes hydrolysis, re-forming anilin and hydrogen peroxide. The anilin thus formed is oxidised back again to nitrobenzene, and the action is thus reversible:—



As the hydrogen peroxide is continually at work as well as being continually re-formed, the rapid deterioration of the solution is prevented.

**Nitrosobenzene** is more probably the oxidation product. It is well known that Caro's Acid (a compound of  $H_2O_2$  and  $H_2SO_4$ ) oxidises Anilin to Nitrosobenzene thus:— $C_6H_5NH_2 + 2H_2SO_5 = C_6H_5NO + 2H_2SO_4 + H_2O$ . The product might revert again by interacting with water, but this is doubtful.

Acetanilide alone does not seem to preserve  $H_2O_2$ . A specimen containing 0.024 Gm. per 100 Cc. ( $=\frac{1}{3}$  grain per ounce approx.), on neutralising with calcium carbonate rapidly lost its strength. The original did not appreciably lose strength but became yellow and smelt similar to nitrobenzene.—H. Finnemore, P.J. i./14,421.

Further references on this subject.—P.J. i./14,275,390.

## HYOSCINA.

### CRIPPEN POISONING CASE.

Hawley Harvey Crippen was convicted on October 22nd, 1910, of having poisoned his wife with Hyoscine Hydrobromide 5 grains of which he had purchased. Dr. W. H. Wilcox found altogether  $\frac{5}{4}$  grain of Hyoscine, equivalent to  $\frac{2}{3}$  grain of Hyoscine Hydrobromide, and he expressed the opinion that there must have been more than  $\frac{1}{2}$  grain in the body as a whole though far more than that had probably been used. The sales were made as retail sales and recorded in the Poisons Book kept for the purpose. '*The fact that a purchaser was a medical practitioner, whether registered or not, does not necessarily convert the sale of a poison by a retailer into a wholesale transaction.*'

(*Retailers should err on the safe side in the sale of Part I. Poisons*).—(C. and D.).

There was some uncertainty as to how the Hyoscine was administered—Crippen stating that he had made it into Tablets for his patients by impregnating ready-made sugar discs with the medicament. There appeared to be the general assumption in the case that Hyoscine is little used except in mania—this is, of course, very far from the facts, *vide* 'Uses' Vol. I. p. 436.

It is the only drug described as useful in certain forms of erethism-urethritis—in doses of  $\frac{1}{200}$  grain twice daily. White and Martin's "Genito-Urinary Surgery," per J. C. McWalter (C.D. ii./10,63).

The mydriatic alkaloid found could have been one of three,—either Atropine, Hyoscine or Hyoscyamine. The alkaloid from all the organs under examination gave definite purple violet colour by **Vitali's Test** (*q.v.*)—turning to a brownish colour. The base was found to be gummy not crystalline. On treating a solution with Bromine in Hydrobromic Acid brown spheres were obtained. Hyoscyamine and Atropine gave crystals with this test.

The distribution of the alkaloid and the fact that the best preserved organs gave the most yield excluded the possibility of its being a ptomaine from putrefaction. The melting points of the Gold Chlorides vary,—that of Atropine is  $148^\circ$ , Hyoscyamine  $160^\circ$ , and Hyoscine  $199^\circ$ , but apparently insufficient for determining the melting point was obtained.

*Refs.*—L. ii./10,1299; B.M.J. ii./10,1372 (complete verbal report of medical evidence). Leader on the subject in which the criminal use of Digitalin, Aconitine, Strychnine, Morphine and Atropine is dwelt upon, as also the current uses of Hyoscine.—B.M.J. ii./10,1451.

It is remarkable that the alkaloid should have remained unaltered so long and in such conditions,—as the material had undergone considerable decom.



position. Strychnine is well known to withstand exposure of all sorts, but it is perhaps unique in this respect; possibly Hyoscine is equally stable, but it remains to be proved so. The question is put as to whether controls had been conducted.—P.J. ii./10,511.

At the time we undertook a control experiment of this kind. On 1st December, 1911,  $\frac{1}{2}$  grain Hyoscine Hydrobromide was dissolved in 1 ounce of Water and mixed with 2 lbs. Minced Cats' Meat; in addition 2 lbs. of the meat were operated upon without addition of Hyoscine, as control. This was left exposed two months; it was then in an advanced state of decomposition—strongly alkaline, of pasty consistence and having a putrid odour, the weight in each case had decreased by about 45%. The two specimens were extracted, with Methylated Spirit, acidified with Acetic Acid (effervescence), the liquids evaporated at about 40° C. to small bulk and extracted with Chloroform in the usual manner. These extractives tested with Alkaloidal Reagents gave the following:—

**Mayer's Reagent** and **Dragendorff's Reagent** gave precipitates with both extractives.

The extractive from the Hyoscine-treated meat gave precipitates with **Gold Chloride** and **Picric Acid**, but the *Control did not*.

Finally the extractive from the Hyoscine-treated-meat gave definite **Vitali's Reaction** which was *not obtainable* in the case of the control. Our result is exceedingly interesting as showing that the Alkaloid Hyoscine remains intact and capable of isolation and recognition whilst in contact with a large amount of animal material undergoing putrefaction for a lengthy period of time.

## IODUM.

The potentialities of **Kelp** as a source of alkaline and other salts—the largest natural source of Potassium and Sodium Salts. Potassium Chloride, Sulphate, Carbonate, Sodium Carbonate, Ammonium Sulphate, Acetate of Lime in addition to Iodine could be profitably recovered.—B.C.D., May 31/1912.

In estimating Iodine in organic Iodine Compounds, it is a good plan to saponify with KOH 2 Gm. Water 12 Cc. and Alcohol 30 Cc. After cooling place in separator and make acid with  $H_2SO_4$ ; add Chloroform and then a few drops of  $NaNO_2$  Solution. Shake and withdraw the Chloroform, and then add a little more  $NaNO_2$  and more Chloroform, and so on until all Iodine is removed. Wash with water, add  $NaHCO_3$  and titrate with  $N/10 Na_2S_2O_3$ .—P.J. ii./11,711, *c.f.*, Thyroid Gland, Martindale's estimation process.

**Limit of Color produced by Iodine visible in Carbon Disulphide, and in Chloroform and Ether:—**

In Carbon Disulphide and Chloroform we found decided mauve color is visible in 1 in 500,000 solution. In Ether the brown colour is visible in the same dilution.

## ESTIMATION OF THE 'IODINE NUMBER' OF A FAT OR OIL.

In the following method Chlor-Iodine addition products are formed of the glycerides of the unsaturated fatty acids and the acids themselves that are contained in the oils so treated.

The Iodine Number indicates the percentage of iodine capable of absorption. Hübl's Iodine Solution is prepared; Dissolve Iodine 25 Gm. in absolute Alcohol, 500 Cc.; dissolve Mercuric Chloride 30 Gm. in a further 500 Cc. of Absolute Alcohol, filter and add to the first solution. Allow to stand twelve hours or so, and ascertain the strength of iodine by a standard sodium thiosulphate solution in the customary manner.

0.8 Gm. of the fat, or 0.3 Gm. of a drying oil, or 0.4 Gm. of a non-drying oil is accurately weighed out and dissolved in 10 Cc. of chloroform. To the solution in a stoppered vessel 20 Cc. of the Hübl's Solution are added, and if the mixture becomes decolourised on standing a short time a further 10 Cc. or Hübl's Solution are added. Then add 10 to 15 Cc. of Solution of Potassium Iodide 10% and dilute the whole with 150 Cc. of water. Determine the free iodine with thio-sulphate and starch, shaking thoroughly. Conduct a blank experiment with the same quantities of chloroform, iodine, &c., deduct the

quantity required in the original experiment from the volume of the thio-sulphate solution used in this blank experiment and calculate into the equivalent of iodine—this again is to be calculated into units per cent. of the oil.

Example.—0·8 Gm. of a fat required 36—7 Cc. of Thiosulphate Solution=

29 Cc. =  $0\cdot3561$  Gm. Iodine, therefore 100 of the fat combines with  $\frac{0\cdot3561 \times 100}{0\cdot8}$

Iodine = 45·6 which is therefore the Iodine Number of the fat.

#### IODINE NUMBERS OF CERTAIN OILS AND FATS.

Almond Oil 93—101·9.	Maize Oil 111—122·9.
Apricot-kernel Oil 100—108.	Neatsfoot Oil 62—72.
Arachis Oil 85·6—105.	Olein (pure) 81·7.
Cacao-butter 34·0—37·7.	Olive Oil 77·28—88.
Castor Oil 83·4—85·9.	Poppy Seed Oil 132·6—143·3. We
Coco Nut Oil 9·5 (but see also <i>Vol. I</i> , p. 83.	found recently 138·1.
Cod-liver Oil 126—141.	Sesame Oil 102·7—112.
Cottonseed Oil 102—116·9.	Rape Seed Oil 97—106.
Human Fat 61·5.— <i>L. ii./07,691.</i>	Soya Oil 121·3—123·2. ( <i>Vide</i> also <i>Vol.</i> <i>I</i> , p. 849. We found recently only
Japan Wax 4·2—6·6.	80·8, a doubtful sample.
Lard 46—63·8.	Sperm Oil 81·3—85.
Linseed (boiled) Oil 73·7—101·3.	Sunflower Seed Oil 119·7—135. We
Linseed (raw) Oil 170—187·7.	found recently 136·1.

Fats dissolve more than 5 times as much nitrogen as an equal volume of water or blood plasma. Caisson disease depends on this.—*L. ii./07,691*

Comparative examination of the Halogen absorption of oils by Hübl's and other methods; the bromine method of McIlheney is better than the iodine ones.—*P.J. ii./09,146,201.*

Halogen Compounds of fatty acids formed by Hübl's Reagent.—*P.J. ii./11, 437.*

## ORGANIC IODINE COMPOUNDS (*c.f.* IODINE CHAPTER, VOL. I.).

The amount of Iodine in Organic Iodine Compounds (except in the case of Iodipin which is generally considered the most efficacious of these—is far less than that prescribed in an ordinary dose of alkaline iodide,—they are only non-toxic by reason of the small amount of the element they contain.

### Approximate amount of Iodine in daily dose:—

Potassium Iodide	.. .. .	22·9	grains.
Iodalbin	.. .. .	6·45	„
Iodoglidine	.. .. .	2·25	„
Sajodin	.. .. .	14·5	„
Iodipin	.. .. .	18·0	„
Olivinol Iodate (a product similar to latter, but made from Olive Oil)	.. .. .	11·4	„
Tlodine	.. .. .	2·25	„
Iodival	.. .. .	7·05	„

Note that although 65 to 80% of the Iodine may appear in the urine in 24 hours when Potassium Iodide is given by the mouth, this leaves a considerable residue, say 7 grains, with a daily dose of 30 grains—or more than the total contained in most of the organic compounds.—*B.M.J. ii./10,1597, c.f. also Bromine.*

Pharmacological proofs in favour of organic iodides are conspicuous by their absence.—*Jl. A.M.A., Nov., 13/09.*

## IPECACUANHA.

**U.S. Assay Method.**—Shake 15 Gm. of ipecacuanha in No. 80 powder with chloroform, ether and ammonia. A volume of the solution is treated with sulphuric acid, and this solution shaken out with ether in the presence of ammonia. The ether-soluble alkaloid thus obtained is dissolved in N/10 sulphuric acid, warming gently if necessary. The acid solution is then back-titrated with alkali, using Cochineal as indicator, and employing the factor 0·0238 to ascertain the percentage of alkaloids. (1 Cc. N/10 Acid = 0·02314 Gm. Cephaeline or 0·02453 Gm. Emetine—a mean of 0·0238, *c.f. infra*).



The factor is an arbitrary one, based on assuming that emetine and cephaeline are in equal proportion. Cochineal (as above directed) is better than hæmatoxylin.—A. B. Lyons, Int. Cong., 1909.

Unworkable as the acid liquors are difficult to filter.—Am. Jl. Ph., 1906, 454.

Methods of assaying with results: Brazilian, alkaloidal content about 2.2% Carthagena about 2.0%.—P.J. i./03,425; ii./04,475.

Assay and identification of the powdered root.—P.J. ii./03,73,101.

Review of the current methods of estimation. Titration of the residue should be insisted upon.—P.J. ii./05,124.

Ipecacuanha Alkaloids are fairly uniform, generally from 2 to 2.5% (soluble in Chloroform). Umney.—C.D. ii./08,492; P.J. ii./09,344.

Colour reactions of the alkaloids similar to those of morphine.—Y.B.P. 1903, 96.

Paul and Cownley stated the average composition of Rio and Carthagena alkaloids to be,—Emetine in Rio 72 per cent., in Cathagena 40.5%; Cephaeline in Rio 25.9, Carthagena 56.8%. Recent examination of Carthagena infers a larger proportion of Emetine or of some other base of high molecular weight.—Evans Anal. Notes, 1912.

### **Extractum Ipecacuanhæ Liquidum (Off.).**

The separation of the total alkaloid into emetine and cephaeline by Pateron's process would exclude the use of Carthagena Ipecacuanha. The cephaeline should not exceed 30% of the total.—B. & C.D. i./05,403.

W. B. Cowie finds the following process to yield higher results than the B.P. ('98) and the product is purer.

Ten Cc. of Liquid Extract are evaporated in a flat basin with 5 Cc. of  $\frac{N}{1}$

Acetic Acid and 10 Cc. of Water to 5 Cc. Twenty Cc. of water are added with 5 Cc. Acetic Acid and the resinous matter broken up and remove by filtering through a pledget of cotton wool into a cylinder. The capsule is washed with 10 Cc. water and 1 Cc. Acetic Acid. To the cold mixture is added 1 Cc. liquor ferri dialysatus (1885), the whole made up to 50 Cc., well shaken and set aside to separate.

Twenty-five Cc. are filtered off into a separator, mixed with excess of Ammonia and 20 Cc. of equal volumes of ether and chloroform, well agitated, warmed and set aside to settle. This extraction is repeated with another 20 Cc. of ether and chloroform mixture. Other two extractions are made with 10 Cc. of chloroform, which gives a more complete extraction. The bulked liquids are distilled off and the residue dried at 80° C. until weight is constant.

The weighed residue is dissolved in excess of N/10 HCl and back-titrated with N/20 NaOH, using tincture of cochineal as indicator.—P.J. i./13,433. 1 Cc. N/10 HCl. = 0.02865 Gm. combined or mean of emetine and cephaeline according to new formulæ (Vol. I., p. 486 and 489).

## **JABORANDI FOLIA**

*P. Microphyllus* is largely used in making pilocarpine and is official in U.S. if yielding not less than 0.5% alkaloids; it may yield 0.6%.

FR. CX. directs *P. Jaborandi* to be used, but states that *P. Pennatifolius* is much employed. It states further that *P. Microphyllus* Stapf. (Maranham Jaborandi) is esteemed by manufacturers on account of its high alkaloid content, but is the most adulterated.

U.S. Pharmacopœia Revision Note.—Replace the percolation process in the assay method by the aliquot part method.—Am. Jl. Ph., Nov. 1911, 525.

*P. Pennatifolius*, *P. Sellowianus*, and *P. Trachylophus* are substitutes and differ from the leaf as described in B.P. '98.

*P. Trachylophus* contained as much as 0.75%.—Southall's Lab. Rep.

*P. Ricemosus*.—Jowett and Pyman obtained Pilocarpine Nitrate = 0.12 per cent. of the leaves but no other crystalline constituent (contrary to previous workers).—Proc. Chem. Soc., 1912, 28, 268.

**Pilosine.**—A new alkaloid from *P. Microphyllus*—from the mother liquors after separating Pilocarpine and Iso-pilocarpine. Content 0.007%.—Proc. Chem. Soc., 1912, 29, 267.

### **Pilocarpinæ Nitræs.**

For an aqueous solution of 2 Gm. in 100 Cc.  $a_D = +82.2$  @ 18° C.—FR. CX. Pure Pilocarpine Nitrate melts at 177–178° C. ④ Isopilocarpine Nitrate

(the salt of an isomeride and conversion product of Pilocarpine) melts at 159°C. P.J. i./97,466; i./04,54. That in U.S. melts at 170·9° C. FR. CX. 177° C.

For further information see.—J.C.S.T., 1900,77,473; 1901,78,580,1331 1903, 83,438; Y.B.P., 1899.

**Detection of Pilocarpine and Quinine in Toilet Preparations.**  
—The relative solubility of Quinine Chromate and insolubility of Pilocarpine Chromate is used —P.J. ii./12,317.

## JALAPÆ RESINA.

Power made various Extractives of Jalap Resin—with petroleum, ether, chloroform, ethyl acetate, and alcohol—all of these excepting the first produced purgation of dogs. He concludes that none of the amorphous bodies obtained from Jalap should have chemical formulæ assigned to them. —P.J. ii./09,7.

The ether test for scammony was devised to detect the adulteration with jalap. Scammony resin of commerce is obtained from the roots and not from the gum resin. American Scammony called '*Orizaba Jalap Root*' (*Ipomæa orizabensis*) is used as the source of the resin.—P.J. ii./05,583.

A sample of this yielded 16 to 20% resin, tested by the Official Process.—C.D. i./08,453.

Further examination of this Mexican Scammony Resin.—P.J. ii./08,366,407.

The so-called Mexican is not equivalent to the product of Levant.—L. i./09,52

Cowie's scheme for valuation of Jalap Resin.—P.J. ii./08,363,405.

## LECITHIN.

Lecithin is a Mono-amino Phosphatide. Phosphatides are complex bodies of more or less fatty nature which can be extracted from tissues by Alcohol, Ether, etc., and which contain fatty acids, Nitrogen and Phosphorus. They are of unstable composition.

On hydrolysis Lecithin yields Stearic Acid, Glycerophosphoric Acid and Choline.—B.M.J. ii./09,677.

Lecithins may be derivatives of either Stearic, Palmitic, or Oleic Acid alone or mixed. Ovo-lecithin is generally assumed to be mainly Stearyl, *i.e.*, Choline-distearo-glycerophosphate, and plant Lecithin to be mainly an Oleic Acid body, but the fatty Acids are not determined with certainty.

### **Lecithin Content of Various Substances in percentages—**

Brain .. ..	16·0	Egg Yolk .. ..	12·0
Heart .. ..	4·5	Peas.. ..	1·2
Liver .. ..	4·3	Lupin Seeds .. ..	2·0
Kidneys .. ..	8·5	Ergot .. ..	1·7
Lung .. ..	1·5	Yeast (dry).. ..	2·0
Spinal Cord .. ..	11·0	Barley .. ..	0·7
Nerve Tissue (dry) .. ..	17·0	Wheat and Rye .. ..	0·6
Blood Corpscles .. ..	0·46	Green Peas .. ..	0·15
Mushrooms .. ..	0·9		

M. 1912.

### **Examination of Lecithin.**

From numerous experiments which we have made both on products of our manufacture **from fresh egg yolk** and on samples obtained from other makers, we recommend the following as tests for purity:—

(1) 1 Gm. should be soluble in 10 Cc. of Alcohol 90%, leaving only a negligible residue not exceeding 2·5%. 1 Gm. dissolved in 10 Cc. of Alcohol should not require more than 0·5 Cc. of N/1 Sodium Hydrate to neutralise (Phenolphthalein).

(2) All the Nitrogen should be present in the form of Choline, *i.e.*, it should be Alcohol soluble.

(3) The total Phosphorus should be estimated. Lecithin should be entirely soluble in Chloroform indicating absence of added mineral Phosphates.



(4) The ratio of Phosphorus to Nitrogen should be approximately 2 : 1.

Phosphorus should be 3·5—3·7%.

Nitrogen should be 1·9—2·0%.

Iodine Value should be 60—65%.

**Lecithin, Determination of in Preparation.**—Extract 1 to 2 Gm. of a Lecithin preparation or 5 to 20 Gm. of a food stated to contain it with 96% Alcohol—first in the cold and then twice under a reflux condenser. Then extract the insoluble portion with boiling Chloroform 2 hours. The combined Alcohol and Chloroform extractives are evaporated and the residues are digested two hours with 100 Cc. Chloroform to separate the Lecithin from Phosphoric Acid, Glycerophosphoric Acid, etc. To estimate Phosphorus Pentoxide in the purified extractive incinerate and oxidise with Sulphuric and Nitric Acids or ignite with Magnesium Oxide and bring to weight as Pyrophosphate in the usual manner. The factor 11·36 is used to convert the amount found of  $P_2O_5$  into Lecithin.—J.S.C.I., 1913, 32, 307, per Y.B.P., 1913, 36.

## LITMUS, CUDBEAR, ORCHIL and TURNSOLE.

**Litmus** *Syn.* **Lackmus** (German) is a blue pigment obtained from *Rocella tinctoria* (*Discomycetes*). Employed chiefly as an indicator for respectively acid and alkali as Litmus Paper, also in form of solution in Volumetric analysis. Litmus is made in Holland by fermenting lichens in presence of ammoniacal liquids and potash. **LITMUS SOLUTION** (B.P. Appendix, 1898).—Boil litmus 2 with alcohol 90% 8 for 1 hour, pour off clear liquid, repeat with 6 and again with 6. Digest the litmus thus washed in distilled water 20, and filter.

In titration, all  $CO_2$  must be removed by boiling before taking end reaction. Not suitable for weak bases. Quinine, Morphine and Strychnine are neutral to it and the acids in their salts can be titrated as if base were absent.—P.J. ii./o8, 194.

Carbon Dioxide only turns Litmus "wine red" when alkaline bicarbonates are present as impurities, otherwise it turns red just like any other acid.—Na. Aug., 1911, p. 215.

**Kübel and Tiemann's Litmus Solution** a modification of the above, is sometimes used. It is prepared as follows:—Extract 30 Gm. powdered Litmus with 500 Cc. of Distilled Water at  $80^\circ C.$ , add Acetic Acid in excess. Evaporate on a water bath to a thick extract. Extract with 100 Cc. 90% Alcohol, then add 50 Cc. more of the same spirit, twice in succession, to remove precipitate from dish. Mix the whole and filter. Wash the filter well with the Alcohol. Dissolve the residue in the filter in distilled water at  $70^\circ C.$ , and dilute to 250 Cc.

**LACMOID** chiefly Diazo-Resorcin Solution 0·2% in Dilute Alcohol.—P.J. ii./o8, 194.

### Cudbear. *Syn.* Red Indigo.

A purplish red powder obtained by the ammoniacal fermentation of *Lecanora tartarea* and other lichens, designated in Germany *Persio*, in France *Orseille de terre*.

The name "Cudbear" is from "Cuthbert," the baptismal name of Dr. Gordon, who in 1777 undertook the management of the manufacture of this dye-stuff (for which he was the patentee) at Leith, and named it after himself.—C.D. i./13, 451.

Excepting for the fact that it is in the condition of a fine powder it is virtually the same article as Orchil.

**Tinctura Persionis.**—P.J. i./o7, 352. Percolate Cudbear  $2\frac{1}{2}$  ounces with 1 pint of a mixture of 90% alcohol 1, and water 2. Used as a colouring agent acids increase the red and alkalis change to purple.

Cudbear, the Examination of.—Orcein is not so useful in Pharmacy as Cudbear.—Am. Jl. Ph., Aug., 1912.

### Archil *Syn.* Orchil.

The word Archil or more properly Orchil was originally the name of the plant from which the dye which goes under the name is obtained. It appears that before the introduction of Archil into this country a similar dye obtained from certain lichens in Scotland was in use under the name "Cork." This is given

in Miller's "Plant Names" (1884) as the name of the lichens yielding Archil.—C.D. i./13,451.

It is made from various lichens, *e.g.*, *Roccella*, *Lecanora*, etc. The lichens are ground up and fermented with addition of stale urine or ammonia. Its production is similar to that used for Litmus except that the Potash is omitted. In commerce it is usually in the form of a pasty mass known as Archil (French, Orseille en pâte).

### Turnsole (Fr. Tournesol).

Daniel Hanbury, in a short paper on the subject, P.J., 1850, 9,308, did much to clear away the mystery regarding the use of this substance, *i.e.*, the colouring of the familiar Dutch cheeses.

The word has been more particularly applied to a product from *Crotophora tinctoria*, A. Juss (Croton *Tinctorium* Linné)—a native of Southern Europe and the Orient. Rags soaked in the juice of this plant are exported to Holland. They change colour on exposure to Ammonia vapour, and this purple colour can be extracted with water for the purpose in question.

Turnsole, by some of the early writers, was supposed to form the colouring matter of litmus (which is not the case, *vide* "Litmus"). Indeed the name may have been associated with Litmus in order to conceal the true nature of this and the U.S.D. XVIII. Edn. and the N.S.D. give Tournesol incorrectly as synonymous with and equivalent to Litmus—for further details *c.f.*, P.B. Powers' Lecture on D. Hanbury, P.J. ii./13,489; C.D. ii./13,514.

PERFUMES OF LICHENS.—In addition to their inherent perfumes lichens have considerable utility as basis of Pot Pourres.—E. M. Holmes, P.R., Dec., 1913.

## MAGNESIUM.

Magnesium is largely used for burning to produce a white light for photographic purposes.

Note, the metal may prove dangerous in certain conditions, *e.g.*, when powdered and mixed with an equal quantity of Silver Nitrate and a drop of water added. Slight explosion with flash may occur. With Mercuric Nitrate there is vigorous reaction, brown fumes rise but no flash.—Na., Nov. 9/11.

Magnesium and Palladium Chloride together in certain proportions will cause water to decompose at ordinary temperature.—Chem. News, May 31, 1912, 253; P.J. ii./12,75.

**Magnesia Mixture** for estimation of Phosphates.

Solution of Magnesium Ammonio-Sulphate. Dissolve Magnesium-Sulphate 20, Ammonium Chloride 40, in Water 160, add Ammonia Solution 84. Allow to deposit in stoppered bottle before use. Employed for the gravimetric estimation of phosphates. Ammonium Magnesium Phosphate is precipitated and converted by incinerating into Magnesium Pyrophosphate  $Mg_2P_2O_7 = 222.64$  I. Wts.

## MALTUM.

**Extractum Malti, Estimation of Diastasic Power.**

The resulting Dextrose may be titrated with Fehling's Solution, 1 Cc. of this = 0.005 Gm. Dextrose = 0.0045 Gm. of Starch converted thereinto.

A properly prepared Malt Extract contains Maltose as its principal ingredient. Glucose and Dextrin are sometimes added as sophistications, and the Protein content is consequently lowered—the latter should be about 6% of the whole, or 8% of the total solids.

The Malt Extracts of Commerce are reported on the total reducing sugar found being calculated as Maltose; the Protein was arrived at from the total nitrogen found. The **Diastasic Power** was expressed as the percentage of Starch digested by the Extract in half an hour at 40° C., *i.e.*, a Diastasic Power of 500 means an extract digesting five times its weight of starch. The percentage of Maltose in the same varied from 53.6 to 75.2, and the Diastasic values from 9 to 413.—B.M.J. ii./09,1477; i./10,30.

Some of the preparations are referred to in our Patent Medicine Chapter.



E. F. Harrison assays Malt Extract by determining the amount of Maltose produced from a given weight using Anhydrous Potato Starch 1 Gm. in Water 100 Cc. with 0.2 Gm. Malt Extract. After half an hour at 40° C. the Maltose formed is titrated. If the Diastasic Power is over 500 repeat the test using less Malt Extract. Glycerin is a frequent addition and might be approved of for an Official preparation to extent of 5% by volume. Proteins might be 5% at least. A lower figure for Protein would point to added Glucose or other non-nitrogenous matter. Added Glucose to be entirely excluded and test for it provided.—P.J. i./09,390; ii./09,148; P.J. ii./10,121,290,330; in answer to Ling—*ibid.*, p. 267,312.

Description of KJELDAHL'S research on the measurement of diastasic power. The action of diastase he showed was influenced by amount of the malt extract present, the temperature of the experiment, the length of time of digestion and the concentration of the solution.—A. R. Smith, P.J. ii./10, 362.

'Diastasic' to indicate the nitrogenous principle, produced during germination of Barley, capable of disintegrating the Starch Molecule, is more correct than 'diastatic.'—C. H. Fielding, P.J. ii./10,312,333.

**Adulterants.**—The principal adulterants found were materials containing dextrose, *e.g.*, starch, syrup and molasses-syrup (from beet sugar). The dextrin formed in mashing of Malt is never much less than 10% of the Maltose formed. The amount of dry solids is determined, the amount of sugar reckoned as Maltose, and the proportion of Nitrogenous substances. If the two latter are added together and deducted from the total dry solids, the result is the amount of non-reducing Nitrogen free Extract, which is practically speaking dextrin, and the figure is called the dextrin figure, usually 9 to 14. If below the minimum one can conclude adulteration with glucose or starch syrup, because the dextrose of these has a much greater reducing power than Maltose. Maltose produces less acidity, *i.e.*, less irritation to the bowels. 70% of Maltose is absorbed in the first hour, whilst only 20—40% of other Sugars. Addition of glucose reduces protein content and the organic phosphorus. The food value of Malt Extract depends directly on its diastasic strength.—Max Hamburg.—P.J. ii./09,133.

#### INCOMPATIBILITY OF VARIOUS CHEMICALS WITH THE DIASTASIC POWER OF MALT EXTRACT.

Preliminary control experiments showed the diastasic power of Malt Extracts of commerce to vary considerably. It is well known that the B.P.C., 1901 method of testing is inclined to be too stringent. A modification of the process consists in the requirement that under the conditions specified 0.5 Gm. of Malt Extract *shall convert its own weight of arrowroot in 20 minutes* (Umney). *This we have found to work satisfactorily.*

Experiments were conducted on lines somewhat analogous with those carried out in the case of Pepsin and Pancreatic Ferments (*q.v.*). Average doses (with some exceptions) of a selected list of the chemicals concerning which the information would prove of value, were mixed with 600 Cc. approx. (actually 24 ounces) of an Arrowroot Mucilage 1% strength and then 30 Cc. (1 ounce) of a 20% malt extract added and the mixtures kept at 100° F. for 30 minutes and examined at 15 and 30 minutes respectively for unconverted starch.

In the following list + indicates complete conversion of the starch—*i.e.*, *such chemicals are compatible with the Diastase of Malt* in conditions approximating those occurring *in vivo*. Indicates Incompatibility.

**Effect of Certain Chemicals on Malt Diastase.**  
(+ *Indicates Compatible.*)

CHEMICAL.	AMOUNT USED.	EFFECT AFTER 15 MINUTES.	EFFECT AFTER 30 MINUTES.
Acetonum .. ..	5 Cc.	+	+
Acid Aceto-Salicylicum .. ..	0·6 Gm.	—	partia
„ Benzoicum .. ..	0·6 Gm.	+	+
„ Boricum .. ..	0·6 Gm.	+	+
„ Carbolicum .. ..	0·2 Cc.	+	+
„ Coumaricum .. ..	0·6 Gm.	+	+
„ Gallicum .. ..	0·6 Gm.	partial	+
„ Hydriodicum .. ..	0·6 Cc.	partial	+
„			(only just so)
„ Hydrobromicum .. ..	2 Cc.	—	—
„ Hydrochloricum .. ..	0·6 Cc.	—	+
„ Hypophosphorosum .. ..	0·5 Cc.	—	—
„ Phosphoricum Dil .. ..	0·6 Cc.	partial	+
„ Sulphurosum .. ..	2 Cc.	—	—
„ Salicylicum .. ..	0·6 Gm.	—	—
„ Tannicum .. ..	0·6 Gm.	—	—
Ammonii Carbonas .. ..	0·5 Gm.	+	+
Caffeinæ Citras .. ..	0·3 Gm.	partial	just
Caffeinæ Sodio-Salicylas .. ..	0·3 Gm.	+	+
Calcii Glycerophosphas .. ..	0·3 Gm.	+	+
Calcii Hypophosphis .. ..	0·3 Gm.	+	+
Chloral Hydras .. ..	0·6 Gm.	+	+
Chloroformum .. ..	0·6 Cc.	+	+
Creosotum .. ..	0·2 Cc.	+	+
Cupri Sulphas .. ..	0·06 Gm.	—	+
Fel Bovis .. ..	0·6 Gm.	+	+
Ferri et Ammonii Citras .. ..	0·5 Gm.	+	+
„ Perchloridi (Liquor) .. ..	0·6 Cc.	—	+
„ Sulphas .. ..	0·2 Gm.	+	+
Formalin .. ..	0·06 Cc.	+	+
Glucose .. ..	15 Cc.	+	+
Glycerinum Pancreatis .. ..	3·5 Cc.	+	+
„ Papain .. ..	2 Cc.	+	+
„ Pepsin .. ..	4 Cc.	+	+
„ Trypsin .. ..	4 Cc.	+	+
Glycerinum .. ..	8 Cc.	+	+
Guaiacol .. ..	0·2 Cc.	+	+
Hydrargyri Perchloridum .. ..	0·0025 Gm.	+	+
Hydrargyri Iodidum (with Potas- sium Iodide) .. ..	0·0025 Gm.	+	+
Hexamethylenetetramine .. ..	0·6 Gm.	+	+
Hydrogenii Peroxidum 10 vols. ..	4 Cc.	+	+
Liquor Donovanii .. ..	0·6 Cc.	+	+
Lithii Citras .. ..	0·5 Gm.	+	+
Magnesi Sulphas .. ..	4 Gm.	+	+
Manganesii Hypophosphis .. ..	0·5 Gm.	+	+
Paraldehydum .. ..	2 Cc.	+	+
Piperazin .. ..	0·6 Gm.	—	—
Potassa Sulphurata .. ..	0·3 Gm.	—	+
Potasii Bicarbonas .. ..	1·2 Gm.	+	+
„ Bromidum .. ..	1·2 Gm.	+	+
„ Chloras .. ..	0·6 Gm.	+	+
„ Hypophosphis .. ..	0·25 Gm.	+	+
„ Permanganas .. ..	0·12 Gm.	—	—
„ Tartras Acidus .. ..	2 Gm.	partial	+
„ „ Neutrale .. ..	4 Gm.	+	+
„ Iodidum .. ..	0·6 Gm.	+	+
Phenazonum .. ..	0·6 Gm.	+	+
Pyramidon (note this alone gives a Violet with Iodine) .. ..	0·3 Gm.	+	+



CHEMICAL.	AMOUNT USED.	EFFECT AFTER 15 MINUTES.	EFFECT AFTER 30 MINUTES.
Phosphorus .. ..	0·0013 Gm	+	+
Quininæ Hydrochlor .. ..	0·3 Gm.	+	+
"    Bi- .. ..	0·3 Gm.	+	+
Sodii Nitris .. ..	0·06 Gm.	+	+
Syrupus Eastoni .. ..	2 Cc.	+	+
"    Ferri Iodidi .. ..	2 Cc.	+	+
"    , Phosphatis .. ..	2 Cc.	+	+
Terpinol .. ..	0·2 Cc.	+	+
Thymol .. ..	0·1 Gm	+	+
Tylmarin .. ..	0·6 Gm.	+	+
Zinci Bromidum .. ..	0·12 Gm.	+	+
"    Sulphas .. ..	0·12 Gm.	+	+

The following gave—in *stronger proportion*, viz., average dose in *only 150 Cc. (5 ounces)* of the fluid the effects indicated :—

CHEMICAL.	AMOUNT USED.	EFFECT AT 30 MINUTES.
Acid Aceto-Salicylicum .. ..	0·6 Gm.	—
"    Benzoicum .. ..	0·6 Gm.	—
"    Gallicum .. ..	0·6 Gm.	—
"    Hydriodicum .. ..	0·6 Cc.	—
"    Hydrochloricum .. ..	0·6 Cc.	—
"    Phosphoric Dil .. ..	0·6 Cc.	—
Caffeinæ Citras .. ..	0·3 Gm.	—
Glycerinum Pepsini .. ..	4 Cc.	—
Cupri Sulphas .. ..	0·06 Gm.	—
Ferri Perchloridi Liquor .. ..	0·6 Cc.	—
Potassa Sulphurata .. ..	0·3 Gm.	—
Potassii Tartras Acidus .. ..	2 Gm.	—
Syrupus Eastoni .. ..	2 Cc.	—
Zinci Bromidum .. ..	0·12 Gm.	partial
"    Sulphas .. ..	0·12 Gm.	—

It will be seen therefore that the following in general are **incompatible** with Malt Diastase.

Acids,—various, Inorganic and Organic, and Acid preparations :—

Ferri Perchloridum,

Pepsin preparations,

Piperazin,

Potassii Permanganas.

And that a very large number of substances which might have been expected to have decided inhibitory action on the ferment are apparently *compatible* and may hence be prescribed simultaneously when required. *c.f.* also Enzyme Action, Vol. I. p. 601.

Free Ammonia (not included in our list) is stated to inhibit Malt Diastase.

### MEL DEPURATUM (Off.).

The honey of commerce melted on a water bath and strained hot. Now directed "to be adjusted to Sp. Gr. 1·36 if necessary."

P.G.V. gives the following tests.—An Aqueous Solution (Honey 1 and Water 2) should have Sp. Gr. of at least 1·11. It should yield only slight

precipitates with Silver Nitrate and Barium Chloride, and on mixing with an equal volume of Ammonia should not at once change colour (*foreign colouring matter*). 5 Cc. of the Solution treated with a few drops of Concentrated HCl must not turn pink or red (*Azo colours*). 15 Cc. of the Aqueous Solution warmed on a water bath and treated with 0.5 Cc. of Tannin Solution (1 in 20) and filtered—1 Cc. of the cold filtrate (clear) on addition of 2 drops of Fuming HCl and 10 Cc. of Absolute Alcohol should not turn milky (absence of *Starch mucilage* and *Dextrin*).

For neutralisation 10 Gm. of Honey after diluting with 5 volumes of water shall require at most 0.5 Cc. N/1 KOH, using Phenolphthalein as indicator—(Test for *rancid honey*).

Honey on incineration should yield not less than 0.1 or more than 0.8% residue (*Invert Sugar and Starch*).

U.S.P. gives the following :—

If 2 Cc. of pure Concentrated Sulphuric Acid be placed in a test tube 1 cm. in diameter and 0.5 cc of Honey Solution (1 to 4) be allowed to flow upon it so as to form a distinct upper layer, no coloured line of contact should show at once, and at the end of an hour the zone of contact should be at most yellowish or clear brown. A brownish colour becoming nearly black at the end of half an hour should not develop.

### Morphine *see* Opium.

## NITROGLYCERINUM.

### Assay of Nitroglycerin in Solutions and Tablets.

Pure fused Potassium Nitrate 0.722 Gm. is dissolved in Distilled Water, *q.s.*, to 1,000 Cc. and used as standard. One Cc. of this solution contains 0.0001 Gm. Nitrogen in form of Nitrate—thus 1.2 Cc. will contain the same amount of Nitrogen as  $\frac{1}{100}$  grain of pure Nitroglycerin. If an Alcoholic Solution be the subject of analysis the equivalent of 0.00065 Gm. ( $\frac{1}{100}$  grain) of pure Nitroglycerin (calculated) is measured out and allowed to evaporate spontaneously in a dish and in another dish 1.2 Cc. of the standard is measured and evaporated at a low heat. When both are dry 2 Cc. of Phenol-disulphonic Acid Reagent are added to each—both are well stirred and left 10 minutes, diluted with water, rendered slightly alkaline with KOH and diluted to 100 Cc. or less in Nessler tubes and compared. For Tablets, 5 tablets are powdered, dissolved in 10 Cc., filtered and 2 Cc. of the filtrate (or equivalent of  $\frac{1}{100}$  grain) treated as above.

**Phenol Di-Sulphonic Acid Reagent.**—Heat Phenol 3 Gm. with Sulphuric Acid 37 Gm. in a flask on a water bath at or near 100° C. for 6 hours. —Sutton's Volumetric Analysis.

We have found the method to give concordant results with Alcoholic Solutions of Nitroglycerin, but it is not suitable for the Tabellæ as made by the writer.

## NUTRIMENTA.

**Foods** may be classified as follows:—

### 1. Proteins. (a) free and (b) combined.

(a) These include the Albumins and Globulins and the results of proteolysis of these, viz., Albumoses and Peptones.

(b) These contain Hæmoglobin, which is an albuminous compound with a complex iron body; Glycoproteins, which are compounds of proteins with carbohydrates; Nucleoproteins, which are compounds of proteins and Nucleic Acid, which latter is an organic compound of Phosphoric Acid.

The decomposition of proteins produces the nitrogenous extractives, *i.e.*, Urea, Purin or Alloxuric bodies, such as Xanthin, Hypoxanthin and Uric acid, Creatin and Creatinin.

**Fats.** This group of proximate principles of the tissues, is represented by the glycerides, triolein, tripalmitin and tristearin (*v.p.* 125). Here is to be included also Lecithin, which on hydrolysis yields glycerophosphoric acid and Choline—the latter is an alkaloid allied to Neurine, and when in excess is a sign of nervous tissue degenerating and will produce toxic symptoms when existing in quantity in excess of the amount which can be oxidised into urea.



3. **Carbohydrates.** These may be in part decomposition products of the proteins and in part material about to be dealt with by the bioplasm, they are Monosaccharides,  $C_6H_{12}O_6$  (Glucose, Galactose and Mannose), Disaccharides  $C_{12}H_{22}O_{11}$  (Cane Sugar, Milk Sugar, and Maltose), Polysaccharides  $(C_6H_{10}O_5)_n$  (Glycogen, Starch, and Cellulose).<sup>\*</sup> They are all converted into glucose in the body, whilst they are also stored up as glycogen or animal starch pending metabolism in the liver, muscles, &c.—“Nutrition and Malnutrition.”—Allchin, L. i./05,1111.

### Biuret Reaction.

This reaction is used as one of several general reactions for albuminoid substances.

It is used in particular to recognise Urea, which heated in a capillary tube, until the melted Urea is distinctly turbid and dissolved on cooling in water with a few drops of Soda Solution added, gives, on adding a drop of dilute Copper Sulphate Solution, a red to violet colour, which turns to blue on further addition of the Copper Solution.

To obtain good results with this test in the recognition of Protein, the test solutions of Albumin, Copper Sulphate and Sodium Hydrate are best of following strengths :—Albumin in Distilled water 0·2%, Sodium Hydrate 1 Gm. in 10 Cc., and Copper Sulphate 5 Gm. to 100 Cc. water. Limits of delicacy both with this and cold Nitric Acid are given.—Bio. Chem. Jl., Vol. IV. ; L. ii./09,302.

**Proteins, Nomenclature of.** Desirability for revision. I. ‘Proteid’ should be rejected. II. ‘Protein’ is recommended. If used at all the word ‘Albuminoid’ to be viewed as a synonym of Protein. III. The sub-classes to be protamines, histones, albumins, globulins, sclero-proteins, phospho-proteins, conjugated proteins, derivatives of proteins, polypeptides. IV. The term ‘Caseinogen’ to be used for the principal protein in milk and Casein for its derivative,—the result of action of rennet. V. The two principal proteins of the muscle plasma to be called paramyosinogen and myosinogen,—soluble myosin to take the place of v. Fürth’s soluble myogen fibrin. The term myosin to be restricted to the final product formed during rigor mortis.—L. i./07,672 ; P.J. i./07,288.

For further remarks on the Classification of Proteins, *vide* Allen, 4th Edn., Vol. VIII., p. 33.

The analysis (hydrolysis) of Proteins gives glycocoll, alanine, leucine, etc.,—amido-acids. Fischer, starting with glycocoll, has synthesised 100 bodies closely allied to peptones,—he designates them ‘polypeptides’—the work gives biology a clearer insight into the chemistry of animal and plant life. Synthesis of enzymes is also possible.—P.J. i./07,260 ; Am. Jl. Ph. April, ’07,168.

**AMIDO-ACIDS.** *Syn.* AMINO ACIDS.—These are very important constituents of Proteins. They are acids containing the Amido ( $NH_2$ ) group. It has been suggested that all proteins are derived from Aspartic Aldehyde by condensation. They are both basic and acidic, *e.g.*, the following :—

- Carbamic Acid  $NH_2.COOH$ . (Amido-formic Acid.)
- Glycocoll  $NH_2.CH_2.COOH$ . (Amido-acetic Acid.)
- Sarkosin  $CH_3.NH.CH_2.COOH$ . (Methyl-glycocoll.)
- Alanine  $CH_3NH_2.CH.COOH$ . (Amido-propionic Acid.)
- Leucine  $CH_3.(CH_2)_3.CH(NH_2).COOH$ . (Amido-caproic Acid.)
- Aspartic Acid  $HOOC.CH_2.CH(NH_2).COOH$ . (Amido-succinic Acid.)
- Glutarminic Acid  $HOOC.(CH_2)_2CH.NH_2.COOH$ . (Amido-glutaric Acid.)
- Tyrosine  $HO.C_6H_4.CH_2.CH(NH_2).COOH$ . (Hydroxyphenyl-amido-propionic Acid.)
- Taurine  $NH_2.CH_2.CH_2.SO_3H$ . (Amido-ethane-sulphonic Acid.)

<sup>\*</sup> NOTE.—Importance of removing Carbohydrate matter from the teeth. Many organisms in the mouth ferment, Carbohydrates producing chiefly Lactic Acid. MONOSACCHARIDES are the most readily fermented. DISACCHARIDES require to be first inverted to MONOSACCHARIDES by an enzyme formed by certain of the mouth organisms before Lactic Acid can be produced. STARCHES require a double inversion—the first stage brought about by ptyalin or organisms before fermentation to an acid can occur. Formulæ are given showing that 1 mol.  $C_6H_{12}O_6$  (glucose) produces 2 mols. Lactic Acid ; 1 mol. of the Disaccharide Cane Sugar  $C_{12}H_{22}O_{11}$  + 1 mol.  $H_2O$  gives 1 mol. each Dextrose and Lævulose, with ultimate formation of Lactic Acid ; and that the polysaccharide  $(C_6H_{10}O_5)_n$  (Starch) +  $H_2O$  =  $C_6H_{10}O_6$  Dextrin +  $C_{12}H_{22}O_{11}$  Maltose, which Maltose is converted into 2 mols. Dextrose, and ultimately to Lactic Acid. The Lactic Acid dissolves the lime salts of the enamel and a cavity is originated at the point of action.—B.M.J. i./09 396.

At the moment of death proteins change in composition. Dead proteins consist of a mixture of Amido-Acids.—Tibbles *q.v.* for a full account of the theory of Proteins.

The complex molecules of the Proteins have been found to be built up of a number of comparatively simple fractions which can exist independently and which, widely as they differ in structure have in common that they belong almost without exception to the above group of Amido Acids. Some of these fractions are occasional constituents of the excreta, *e.g.*, leucin, tyrosin, cystin in which last the Sulphur of Proteins resides. From others the equally familiar excretory products, or products of putrefaction are derived,—such as Indol from tryptophane, cadaverin from lysin and putrescin from arginin.—A. E. Garrod.—B.M.J. i./11,1413.

Pathology and treatment of diabetes mellitus. Three lectures dealing principally with the physiology of diabetes. Several Diabetic Foods are shown to contain a large proportion of Carbohydrate as starch—these constitute source of great harm. As to drugs something is wanted to set metabolism right in the way that Thyroid Extract acts in myxœdema—but a strong believer in Opium and some of its derivatives.—Pavy.—L. ii./08,1499,1577, 1727.

Further remarks by Halliburton on.—L. i./09,21.

### **Estimation of Amino-Acids in the Urine, *vide* p. 214.**

Protein metabolism during starvation and after giving Milk protein.—L. i./14,236.

### **Diets, effects of various, and the resistance of animals to certain poisons.**

Investigations by Reid Hunt showed by use of Acetonitril  $\text{CH}_3\text{CN}$ , which decomposes into HCN in the body that animals (guinea pigs and mice) when permitted an increased power of oxidation liberate more Hydrocyanic Acid; on the other hand when in a state of partial inanition the intensity of the process of oxidation is lowered, consequently less Acetonitril is decomposed and the animal is rendered more resistant to the poison.

Dextrose, oatmeal, liver, kidney and thyroid gland increased the resistance of mice to the poison. The influence of Iodine compounds and of various articles of diet is due to the power of stimulating the function of the thyroid gland. Certain diets (notably eggs, milk, cheese and various fats) greatly lower the resistance of certain animals to Acetonitril,—their effect is the opposite of that of thyroid. The Pharmacological action of acetonitril renders it useful for such investigations. Most ordinary poisons undergo no marked changes before exerting their toxic effects. Acetonitril, however is, according to general views, poisonous only or largely as a result of formation from it of Hydrocyanic Acid. Formation of Hydrocyanic Acid is due to certain processes of metabolism which may be modified by drugs and diet,—processes of oxidation (by which the Methyl group is oxidised to Formic Acid) are probably involved.

The results of the experiments indicate that there are factors entering into the composition of foods,—more complicated than its Protein, fat and carbohydrate composition and suggest lines of research to find means of increasing resistance of the body to the poisons of disease. Hygienic Lab., Bulletin No. 69, June 1910.—U S. Public Health and Marine Hosp. Service, Washington 1910. *v.* also B.M.J. ii./10 1270.

Aceto-nitrile as a test for thyroid and further feeding experiments.—P.J. i./14,534,599.

### **Food Requirements for Sustenance and Work.—**

The energy demanded by men undertaking a forced march of 25 miles under severe climatic conditions being 5,000 calories (this is calculated on a formula adapted from Zuntz's work,—800 of which calories are furnished by Protein and 1,800 by Starchy Biscuit food) in what form should the remaining 1,400 be furnished?—Melville advocates for soldiers on active service a diet on the following lines:—Proteins 190 Gm. in the form of cheese and leguminous vegetables, Carbohydrates 600 Gm., Fats 150 Gm., and Sugar in the form of jam. He points out that the lack of fat is a serious matter when preserved meat is issued. The proportion of fat to meat in fresh meat is about 1 to 4, but in corned beef this is reduced to 1 to 10. A good form of fat ration is cheese, but lard or suet are also suitable, also a mixture of sugar and jam in equal parts forms an excellent and most sustaining diet.—B.M.J. ii./10,1337.



With regard to Chittenden's statement that "a daily metabolism of 0.10.—0.12 Gm. of Nitrogen per kilogram of body weight is quite adequate for physiological needs, provided a sufficient amount of non-nitrogenous foods is taken to meet the energy requirements of the body,"—this holds good for those leading a sedentary life such as the Bengalis.—B.M.J. ii./10,1341

## CALORIE VALUES OF FOODS.

Hutchison gives the following figures (Calories) as indicating the true worth to the body of the different nutritive constituents as sources of potential energy; Protein 4.1, Carbohydrates 4.1 and Fat 9.3 Calories. Proteins, carbohydrates and albuminoids seem to be oxidized quickly in the tissues, fats more slowly. Therefore, if a rapid output of energy is required, the first group will be more serviceable whereas a slow production over a long time will be equally well met by fat.

**Method of Applying the Calorie Standard.** Multiply the percentage of protein or carbohydrate (or both), that the food contains by 4.1 and the percentage of fat by 9.3 to obtain the total Calories yielded by 100 parts of the food in question.

**Standard amounts of the different nutritive constituents required daily.** Protein 120 grammes, Carbohydrates 500 grammes, Fat 50 grammes. These would yield a total of 3,007 Calories. Such a standard may be regarded as suitable for a man of average build and weight, doing a moderate amount of muscular work; if a greater intake of energy is demanded it should be met by increasing the amount of fat consumed.

### Calorie Values of some proprietary food preparations.

(Except where indicated the Calorie value is between 3.7—3.9).

Allinson's (Dr.) Natural Food.	Granose.
Avenola 3.92.	Grape Nuts.
Chapman's Food.	H.O. (Hornby's Steam cooked Oat-meal) 3.94.
Cheltine Food	Hygiana 4.25.
Dubarry's Revalenta Arabica Food	Nut Bromose 5.10.
3.68 (Consists of Lentil Flour).	Roborat (73% Protein).
Emprote.	Stamina Food.
Eustace Miles' Breakfast Food.	Winter's Prunus Perfect Food 5.17.
Gluten Meal (Either pure gluten or a mixture containing 30% of this).	For full details see B.M.J.i./10,1239.

The above Calorie Values are calculated from the percentage composition and represent the *kilo calories* yielded by complete combustion of 1 Gm. of each food. For comparison are given the—

### Calorie Values (Kilo calories) of a few common foods.

Milk 0.70	Coarse White Bread 3.03
Potatoes 0.98	Fat Beef 3.27
Lean Beef 0.93	Peas 3.31
Eggs 1.59	Lentil Flour 3.55
Cheese 2.4	Fat Mutton 4.03
Fine White Bread 2.74	Butter 8.60
Wholemeal Bread 2.78	Bacon .86

—Hutchison's Food and Principles of Dietetics.—

B.M.J. i./10,1239.

The above commonly accepted *standard of daily food* requirements in adults, as prescribed by Atwater and Voit (Protein 120 Gm., Fat 65 Gm., Carbohydrate 500 Gm.), is thought to be unduly high. Chittenden, for example, says 80 Gm. or less Protein is enough. Investigation into the food requirements of children—to provide nutritious food at small cost.—Chalmers Watson, B.M.J. i./13,603.

### Yeast Extracts as Food.

Yeast extracts, *c.f.*, our Vol. I., p. 254. have been made and substituted for meat extracts; a test has been published for detecting this substitution.—P.J. ii./03,516.704; *vide* also Y.B.P. 1907,101.

The test is based on the fact that Meat Extract contains both creatine and creatinine, whilst Yeast Extract contains neither The "Lancet" (i./07,1505)

believes the test to be a conclusive one if carried out satisfactorily. We have tried the test on Yeast Extract and a well-known brand of Meat Extract and must confess we obtained brownish red colours with both—difficult to distinguish one from the other.

Liquid foods, according to recommendation in America, should contain at least 8·8% solid constituents, and should possess at least as much nutritive power as milk. One-fourth of it, exclusive of Alcohol and Glycerin, should be in the nitrogenous matter. The protein matter should be converted by pepsin or pancreatin—not by acids.—L. ii./07,308.

**Ju-vis** was condemned. Creatin + Creatinine Estimations indicated that it contained only 8% of Meat Extract. Creatin + Creatinine in genuine Meat Extracts is on average 10·85%. It was stated to contain 18% Meat Extract, 21% Yeast Extract and the rest Gelatin, flavouring and water. Yeast Extracts *in toto* are objected to.—Gamgee.—B.M.J. ii./08,449.

Bearing on this controversy the following may be noted :—

“In a recent article Gamgee states that the ingestion of Yeast Extracts involves the enormous increase of Purin bases as compared with an ingestion of meat extracts. The figures he reports are, Purin base, Nitrogen of Yeast Extracts 0·646% of meat extracts 0·433%. Some recent reports by Chapman show that the Purin contents of meat and yeast extracts are practically identical and this agrees with the findings of the writer. There is no conclusive proof of Gamgee's claim that the purin bases of yeast extract are more injurious than those of meat preparations.”—U.S. Dept. of Agriculture, Bureau of Chemistry, No. 62, Nov. 15, 1910. See also A. C. Chapman, B.M.J. ii./08,1741.

Providing correctly (and not wrongly) labelled, Yeast Extracts may be quite good and wholesome in their way. They are practically identical in composition with Meat Extracts and similar in taste. Their presence in Meat Extracts can sometimes be determined microscopically by observing yeast cells. Diluted Fehling's Solution on being brought to the boil after adding a quantity of the Aqueous Solution of the extract to be examined shows a bulky curdled precipitate of greenish grey colour if yeast extract be present.—P.J. ii./11,72.

Yeast as Food.—It has been suggested to use the washed yeast of German breweries. Experiments have shown that dogs assimilate 87·2% of the Nitrogen in the yeast. The slight bitter taste of fresh yeast can be removed by treatment in the cold before drying with Sodium Carbonate.—P.J. ii./11,448

## Hæmoglobin.

### Defibrinated Blood and Globin Solution in treatment of Cancer.—

Experiments by H. C. Ross ('Induced Cell-Reproduction and Cancer,' p. 210) show that *in vitro* cell division is “directly caused by certain constituents of the soluble remains of dead tissues.” In the neighbourhood of old healing ulcers the Hæmoglobin is evidently decomposed,—as the Hæmatin produced in consequence collects as insoluble pigment. When Hæmoglobin decomposes thus into Hæmatin and Globin the former is insoluble in water, except in presence of dilute alkalis. Globin is stated to be readily soluble,—hence this substance (if either of the two) is thought responsible for causing proliferation. A saturated solution of Hæmoglobin on prolonged boiling precipitates the Hæmatin and gives a straw-coloured filtrate which, on evaporation, when reaching saturation point about 4%—becomes deep red. Globin is a protein not precipitated by boiling, decomposing on keeping and giving off a foul smell.

Ross employed this saturated solution at Liverpool in chronic callous ulcers of the leg (simply applied with a little sterile gauze)—granulations set in rapidly and in 20 hours marked effect was seen. Globin has also been used dried in small pieces ‘dotted’ on to the ulcerous surface,—this causes extensive proliferation of the epithelium from the sides of the ulcer, but suppuration is likely to occur, even if the dried Globin is prepared with aseptic precautions. Scabs form which have to be removed with fomentations and the process repeated. A mixture of powdered Globin 5 with Kreatin 2 has also been used and produces more marked proliferation.

This investigation, according to Ross, affords proof that the ‘cell proliferation of healing can be caused by the chemical auxetics Kreatin and Globin.’

**Prevention of Proliferation.**—Normal Blood Serum (*vide ibid* p. 253) has the power of preventing the ‘natural’ auxetics from inducing cell division (Bashford & Murray showed that serum has the power of restraining the growth of



secondary transplanted tumours in mice). Bashford and others also showed that transplanting living growths in mice protect same to some extent against cancer. 'It was considered possible that this (*ibid* p. 254) might be due to the fresh augmented auxetic produced by the transplanted growths giving rise to increase in content of restraining body.' Hence a process of treatment of cancer patients was devised by injecting them with augmented auxetic combined with Blood Serum,—6 ounces of defibrinated sheep's blood being given per rectum every morning. This serum contains the restraining body, and it was thought that the red cells would be destroyed in the rectum, the Hæmoglobin would be decomposed and in time the Globin would become augmented by the action of bacteria present. It was thought that the restraining body of the serum, the auxetic in the globin and in the remains of the white cells, and the products of decomposition would be gradually absorbed and that they might raise the content of the restraining body in the patients—in other words, act as a sort of vaccine. Several cases were treated on these lines—in some with apparent benefit.

Solution of Globin for rectal use has been made by boiling Hæmoglobin of commerce (i.e., Oxyhæmoglobin) and removing the Hæmatin, subsequently adding a small quantity of Sodium Carbonate. This has been prepared 5% strength approx. in 'Globin.' 1 molecule of Hæmoglobin (Allen, *ibid*) is understood to yield two molecules of Globin (the molecular weight of this body being probably about half that of Hæmoglobin)—and 1 molecule of Hæmatin (the molecular weight of which is minute in comparison).

Globin is a histone. Histones are proteins intermediate between protamines and albumins. When oxyhæmoglobin is treated in aqueous solution with dilute acids or alkalis, or when the solution is warmed to 64–69° C. it breaks up into hæmatin and globin.—Allen, 4th Edn., Vol. VIII., 33.

## BREAD AND FLOUR STANDARDISATION.

### Flour Bleaching and Harmful Baking Powders.

The 'Standard Bread' agitation attracted considerable attention early in 1911. We gave the matter most thorough consideration in our last edition (Edn. XV., Vol. II., p. 47), and we still maintain that the Standardisation of Food is *as important as*, if not *more important*, than the standardisation of Drugs which receives every possible consideration. We see no reason for greatly altering what we then said on the matter, excepting perhaps to reiterate its importance and to lay stress on the fact that much of the flour sold in this country is of an *exceedingly poor order*, with little nutritive value and rendering the bread made from it of an unpalatable taste. We incline strongly to the view that poor grades of flour are bleached and otherwise chemically treated to render them white and of good colour, and that these are foisted on to the public, especially the poorer classes. The evil is in our opinion highly discreditable to the controlling Departments. **To mention one evil alone—Bleached Flour in the U.S.A. is prohibited by law for sale in that country, but it is we understand exported for sale here.**

This and similar practices are conducted to make an inferior article look attractive.

Dr. J. M. Hamill's Food Report No. 14, 1911, to the Local Government Board, on the nutritive value of bread made from different varieties of wheat flour gives a useful résumé of the nomenclature of various milling products, *e.g.*—

'Wholemeal' or 'Graham Flour' (actually whole grain flour).

"Entire Wheat Flour" or "Fine Meal"—a product obtained by removing a portion of the bran and grinding the rest of the grain. (This includes so-called "Standard" Flour).

'Households.'—The commercially lower grade of flour obtained from roller mills—it is darkish in color.

'Patent Grade.'—Commercially the higher grade flour produced by roller mills. It is better color than any other grade of flour produced in the mill.

'Straight run' or 'straight grade'—intermediate in appearance and quality between households and patent grades.

**Special flours**, prepared from any of the above usually with the object of improving nutritive qualities.

This report should be read by those making a study of the subject.

One of us (W.H.M.) communicated a short note on the subject of so called Standard Bread to the "Chemist and Druggist" (C.D. i/11, Index Fo. 321) which forms the groundwork to this article. Abstracts from papers by a number of Authorities on Dietetics who have since from time to time written on the subject of "Standard" bread, its advantages and disadvantages, have been incorporated.

The "manifesto" by some of the highest medical authorities defined "Standard" bread as *bread made from unadulterated wheat flour containing at least 80% of the whole wheat including the germ and semolina.*"

A glance at a sectional diagram of a grain of wheat, *e.g.*, as shewn in the above Food Report or on p. 266 in Jago's "Science and Art of Breadmaking" shows the situation of the "germ" (a small portion of the entire grain) in the grain and enables one to understand the reason why it is in great measure winnowed away by the roller process of milling. The husk, or outer envelope yields the bran, and consists roughly of cellulose and salts; the endosperm yields the starch, the germ is rich in protein and fat. With regard to the above definition of "Standard Bread" the word, "Semolina" might as well have been omitted for the reason that it may refer to the most various products according to the fancy of the miller. The semolina obtainable commercially is the hardest portion of the endosperm of the wheat grain and is obtained in a granular form by adjusting the rollers sufficiently far apart, so as not to crush the granules. It is usually prepared from the hardest wheats, *i.e.*, those grown in Southern Europe. The modern roller mills convert the wheat into flour and "offal." Entire Wheat Flour is obtainable from the old fashioned mill stones, or by the roller mills. The germ differs considerably in composition from other parts of the grain. We have placed side by side (from W. Jago—transposed from his figures into percentages) the amounts of certain constituents of a (a) wheat mixture, (b) one of the semolina products—that coming from the second and third "breaks," (c) "Flattened Germ" from the same mixture and (d) Bran:

	Wheat.	Semolina.	Flattened Germ.	Finished Bran.
Moisture ..	38.171	43.041	14.822	22.598
Soluble extract ..	16.403	13.577	43.940	17.567
Soluble protein ..	4.361	3.191	15.652	2.259
Crude gluten (dry)	19.093	19.416	—	—
Ash ..	4.835	3.394	5.501	12.742
Phosphoric Acid ..	2.465	0.747	3.207	7.322
Fat ..	4.993	4.311	11.982	3.068
Cellulose ..	9.671	12.627	4.776	34.4



Note the figures for "*Soluble Extract*," *Protein*, "*Ash*," *Phosphoric Acid* and *Fat* in the *Germ* in comparison with *Wheat*, also the figures for *Ash* and *Phosphoric Acid* of *Bran* compared with those in *wheat*.

With regard to the **mineral constituents in the ash of wheat and other cereals**:—Lime (Allen, 3rd Edn., 1898, vol. 1, p. 447) ranges from 1 to 10% ; Magnesium Oxide gives an average of 12.11% ; Silica rarely reaches 5%, being usually less than 2%,  $P_2O_5$  constitutes an average of 49 to 50%. Iron as  $Fe_2O_3$  averages 1.1%.

We are fully aware that these figures *may* have no value and that it is possible to twist the data into meaninglessness, also that figures giving flour analyses vary with every authority (*c.f.* Atwater and Benedict, Hutchison, Tankard, etc.).

With regard to *bread-making* it may be mentioned that wheat and rye are the only suitable cereals—owing to the fact that they contain the protein "*glutin*" which becomes viscid on mixing with water—hence forming the dough. Glutin is developed by interaction in the presence of water of the two proteins gliadin and glutinin. We are indebted to Nature, May 4/1911, p. 313, for the following remarks.

The outer coats of the grain yield bran, fine pollards, sharps, and middlings, the germ is removed as offal, while ordinary flour is derived almost solely from the endosperm. The flour itself is divided into a larger portion. "bakers" or "households," and a smaller, very white and poor in protein, known as "patents," from which genuine Vienna bread and the best class of fancy breads and pastries are made. The semolina, derived from the central parts of hard wheat, and rich in gluten, is also lacking in white flour.

It will thus be seen that ordinary white flour and white bread made therefrom contain little or none of the bran germ, and semolina, and valuable food constituents—mineral matter and protein of the bran and semolina, and fat and protein of the germ—are lost. Wholemeal bread is therefore richer in the nutritive constituents and has more flavour, but is darker in colour than white bread, owing partly to the inclusion of the bran and partly to an interaction by which dextrin and sugar are formed which undergo darkening in the oven. Wholemeal bread is, however, apt to be irritating on account of the cellulose and silica of the outer coat, but by removal of the outer layers of the husk the irritant material may be excluded, and the valuable mineral, protein, and fatty constituents of the inner branny coat, semolina and germ, retained. Such a flour constitutes the "80 per cent. flour" employed in making the so-called "standard" bread. The term "80 per cent. flour" means that a wheat, a bushel of which weighs 64 lb., yields 80 per cent. flour. In the old method of milling, the wheat is ground between stones, the flour being separated by sifting, and in this way some of the "offal" is retained: hence the term "stone-ground."

There is doubtless some difference of opinion as to the relative values of ordinary and "standard" flour, and the bread made therefrom. The roller mills cleanse the wheat in a very efficient manner. Chemical analysis, except as regards salts, shows little difference between the two; "standard" bread may even be slightly poorer than ordinary bread in protein, owing to the greater percentage of moisture.

Leonard Hill and M. Flack (B.M.J. i./11, 1068) reported on rats fed for three weeks, some on standard bread and some on white bread, and for a second three weeks on white and "standard" flour. The result was astonishing. Of the rats fed on white bread and flour ten died, while only five died of those fed on "standard" bread and flour. The survivors of the latter lot increased in weight  $27\frac{1}{2}$  per cent. against 12 per cent. for those fed on white bread. Another lot fed on white flour *plus* an amount of wheat germ about equal to

that in standard flour, gave results quite as good as for "standard" flour.

In a second note they express the opinion that the State should use all its powers to make wholemeal bread the food of the children of the poor (and ? look after the welfare of the well-to-do by reasonable control of Foodstuff.—W. H. M.). The whole meal is the real staff of life and no saving of trouble or liking "a nice looking loaf" should be the pretext for taking away substances essential for the growth of children. It was found that rats can thrive and be reproductive on wholemeal and water. A diet of white flour and water is more harmful to young rats than old. Germ and bran are needed above all for growth.—B.M.J. i./11,1311.

In a third article they state "standard" flour proved better than wholemeal used in their previous work,—the reason being that the wholemeal previously used contained only a portion of the sharps and bran—their removal gave it a nutritive value higher than the true wholemeal, probably because this contains too much cellulose. *Hovis Flour* contains about 20% of germ. This is separated in the milling by being rolled flat. After screening off it is sterilised and added to white flour. Wholemeal contains about 1 to 2% of germ, 13% of sharps (the inner husk) and 15% of bran. The addition of 20% of germ increases the percentage of protein and insures the presence of the organic Phosphorous compounds essential to growth. The feeding experiments on rats show the *great importance of the germ of which white flour is robbed*.—B.M.J. ii./11,598.

They have shown that rats, mice and pigeons cannot be maintained on white bread and water, *but can live on whole meal or on white bread in which an extract of the sharps and bran in sufficient amount is incorporated*. Bearing on this it is pointed out that a diet of white bread, or polished rice, and tinned food, sterilised by heat, is the cause of beri beri, *i.e.*, demonstrating the importance of certain active principles in the outer layers of wheat, rice, etc. and in milk, meat, etc., which are destroyed by heating to 120° C.—B.M.J. ii./12,601.

W. Tibbles thinks rodents unsuitable animals for the experiments. Cellulose is a *sine quâ non* of proper nutrition to them. There is no doubt whatever about the great nutritive value of the proteins in the germ, but its removal (which is done for the sake of color and keeping qualities) does not rob the bread of much protein. *The total proteins of the grain average 12%,—distributed thus—endosperm 8.925, germ 0.538, aleurone 2.048, episperm 0.178, cuticle 0.362%.* The germ is, however, rich in Nitrogen, *i.e.*, 6.44% including 0.8% Amide Nitrogen (the germ forms, of course, a very small proportion of the entire grain). He holds, B.M.J. i./13,25, that the presence of the cerealin and germ in the flour really increases the total percentage of Nitrogen and Phosphorus very little.

With regard to the Phosphorus in wheat bran,—this was first thought to be inorganic—then to be connected with the nuclein or salts of Nucleic Acid—but researches show that only 33% of the Phosphorus could be accounted for in this way and that the chief



Phosphorus compound is a Magnesium-Calcium-Potassium Salt of a Phospho-organic Acid,—probably identical with Anhydro-oxy-methylene diphosphoric Acid,—an acid which is widely distributed in the vegetable kingdom,—B.M.J. ii./II,861, 1137.

The higher animals are apparently not endowed with power of preparing their own organic phosphorus compounds from inorganic phosphorus, nor indeed, are they probably able to form such compounds of one group from those of another. These bodies are of far-reaching importance to the bioplasm.

It is probable that over sterilisation of preserved meats (*e.g.* temperature of 120°C.) causes deficiency of organic phosphorus.

Rickets has become so common—by comparison—with the German child that in Germany it is called the 'English Disease'—it is less common in the Highlands and in Ireland. The Highland child gets oatmeal containing 0·9%  $P_2O_5$ , mainly in *organic* combination. The Irish child gets probably fresh milk and butter (1%  $P_2O_5$ ) in addition to potatoes which contain a fair amount of Phosphorus near the skins. Light and air may have a good deal to do with protecting both these from rickets. The German child gets rye bread, in this the organic phosphates are evenly diffused throughout, and even fine rye bread contains sufficient (1%  $P_2O_5$ ) of these compounds. He does not suffer from rickets so much as the English child, whose diet is apt to consist largely of *skim milk*, *margarine* (0·03%  $P_2O_5$ ), and *white bread* (0·2%  $P_2O_5$ )—all notably deficient in organic phosphates. At present we use the phosphates of the wheat and rice as food for our prize cattle.—B.M.J. i./II,1421.

A healthy man accustomed to a full mixed diet requires for maintenance of phosphorus equilibrium about 1·5 Gm. of phosphorus, or nearly 3·5 Gm. of Phosphoric Acid per diem; the organic combination seems to be the best. The calcium requirement is equivalent to about 0·7 Gm. of Calcium Oxide *per diem*.—Na., Dec. 1, 1910, p. 148.

W. Tibbles writing again says: "In addition to the Cellulose, the Amino-Acids (Asparagin, Leucin and Tyrosin) are of importance. It is to the greater amount of these in the germ and cereal in that one may look for the different effects obtained by feeding with flours of various grades.—B.M.J. ii./II,1137.

In a further note L. Hill and M. Flack write: "Wheat germ alone added to white flour makes this an adequate food on which animals can live healthily. This proves that the lack of Cellulose has nothing to do with the insufficiency of white flour, and that whatever the active principle may be, it is present *no less in germ than in bran and sharps*. In fact, rats did better on white flour plus germ than on white flour plus sharps, bran, and a trace of germ.—B.M.J. ii./II, 1330.

Robert Saundby communicated a paper on food and feeding which bears on the subject (B.M.J. i./II,1218). The following is an abstract from this communication:

The public were asked to adopt the view that 'white bread' is

deficient in nitrogen and inferior to bread made from flour containing the whole of the constituents of the grain. **Wholemeal or Graham Flour.**—No objection can be made against white bread so long as this is not due to chemical bleaching. (For the subject of bleaching, *vide* later). It must contain weight for weight as good proportions of protein, carbohydrate, mineral matter and fat as the 'standard' article. An undesirable effect of the agitation was the unloading of large stocks of inferior flour (*Truth*, April 12, 1911, p. 207). The moisture in bread varies from 30 to 40%. In Columbia, U.S.A., the proportion is regulated by law to 31%, but here there is *no legal limit*. Excess of gluten produces a loaf that retains moisture. Beri Beri (*vide* also *Vol. I.*, p. 838, *Vol. II.*, p. 283), seems to be associated with eating completely shelled rice. Something is removed in the 'polishings' which is of great importance, and there may be something of the same kind in the case of white flour. It has been brought forward that DENTAL CARIES is attributable to the softness of white bread, but 'standard' bread is just as soft, and the natives of South Africa, India and Japan, subsist on soft starchy foods and have good teeth. Caries is more likely to be due to excessive consumption of sugar, which rose from 30 lb. per head in 1864 to 89 lbs. per head in 1910. The importance of doing away with hand labour for machine-made bread is strongly urged in the interests of hygiene and health. *The present conditions of many bakehouses which are overheated cellars filled with half-naked men from whose bodies sweat pours to mingle with the dough is not pleasant to think of.* A baker is stated to lose 200 to 340 Gm. in weight while kneading a batch of bread, mainly in perspiration, part of which certainly enters into the dough.

The therapeutic value of FASTING is carefully considered in this paper. Disappearance of or amelioration of many chronic ailments in Rome after fast has been proved; prison diet has been shown to have similar effect. A fasting day from time to time in treating diabetes has been proved of value and so on. There is no doubt as to the high nutritive value of oatmeal and porridge.

#### **Increase in acidity of Bread during Mastication.**

Hill and Flack conducted some experiments on this subject. They did not find any marked difference between the acidity produced on masticating white and wholemeal breads (it has been said that decay of teeth is due to acid production from white bread). Thomas Read writes: "It would appear as if the ferments from the wheat germs in the wholemeal bread used by Leonard Hill had been injured before bread making—then both breads would form acid in the same way in mastication. If the ferments in the 'Standard' type have not been injured before baking, the conversion of starch into grape sugar takes place during bread making, and no acid is formed during mastication. If, on the other hand, the flour does not contain the ferments of the wheat germs or they have been injured no conversion of starch into grape sugar takes place during bread making, and when the bread reaches the mouth the ptyalin of the saliva converts starch into grape sugar and bacteria in the



mouth convert this freshly formed sugar into lactic acid which decays the teeth."—B.M.J. i./11,1456.

W. A. Bond pointed out that *flour of the 'Standard' type must contain more protein, fat and ash, than fine white flour made from the corresponding wheat or mixture of wheats.* He suggested a standardising method based on the presence of a substance of the nature of Phytin, also a minimum of protein, etc.—L. i./11,1669.

Benjamin Moore writes "*anent the Phospho-protein in the sub-pericarpal layers of grain,*" that this is a glucoside—possibly galactosan. These glucosides are known as hemi-celluloses and are termed pantosans and galactosans according as they yield a pentose or galactose on hydrolysis. Polyneuritis established in fowls by feeding on polished rice can be combated by a daily ration of an alcoholic extract of the rice meal from the separated pericarpal layers, containing only 0.16 mgr. of Phosphorus Pentoxide and 4 mgr. of nitrogen.—B.M.J. ii./11,1137.

### **Bleaching of Flour.—**

The bleaching of flour by chemical process is one of the crying evils, and, of course, unnecessary. It is safe to say that if the agitation did nothing more than rouse those in authority to the necessity of stopping bleaching, its work was rewarded.

The United States Government in 1910 took action against certain flour-millers in regard to 625 sacks of flour which were alleged to be adulterated, and after trial the Government authorities proved their case and the flour was condemned. It had been bleached by the 'Alsop' process. "The essential apparatus in this process is a small chamber with two electrodes. One of these electrodes is stationary; the other is raised up and down by a suitable crank motion, so as to approach the first. These electrodes are charged with a heavy current of electricity. When the points of the electrodes touch, the current flows just for a second, and when they are pulled apart a flaming discharge takes place between the two. This discharge is of a high temperature—so much higher than the ordinary temperature of combustion that it causes the nitrogen and oxygen in the air to combine, actually to burn, one might say, and the result is nitrogen peroxide. While the electrodes are in operation, a current of air sweeps out the nitrogen peroxide, and a further supply of air is drawn in. After being swept along, the nitrogen peroxide is carried by a tube to a box, which is provided with a rotating apparatus. To this box, called an agitator, comes the finished flour from the mill, and is made to fall down through the nitrogen peroxide and air. During this passage the bleaching is effected."—From a bulletin on the case by the U.S. Dept. of Agriculture.

The result of this process is that the flour contains an appreciable amount of nitrites. The C.D. i/11,512 described the physiological effect of this flour as 'disastrous' in the case of many persons who eat bread made from it.

To this criticism we would add further criticism. What we say

is that the Bleaching of Flour should be an *unnecessary proceeding and should not be tolerated*.

In a Local Government Board Report (Food Report No. 12, 1911) Drs. J. M. Hamill and G. W. Monier-Williams dealing with the action of Nitrogen Peroxide ( $N_2O_4$ ) (in quantities up to 300 Cc. per 1 kilo flour) indicate that the color of the bleached flour may change again, *i.e.*, become yellow or still more bleached according to circumstances. The quantity of Nitrous Acid or Nitrites formed is proportional to the  $N_2O_4$  used. The  $N_2O_4$  is present in the flour as Nitric and Nitrous Acids or Nitrates and Nitrites. In highly bleached flour (1 kilo with 300 Cc. of  $N_2O_4$ ) an increase in the amounts of soluble Proteins and soluble Carbohydrates takes place. The amount of soluble Nitrogen is doubled (due entirely to the solubility of Gliadin in  $HNO_3$  of certain strengths). About 6 to 7% of the Nitrogen introduced as  $N_2O_4$ —is absorbed by the fat of the flour—it undergoes change like an oxidised oil. The rate of digestion was greatly retarded if the starch had been previously treated with  $N_2O_4$ . *Bleaching exercised an inhibitory effect on the salivary digestion of flour.*

In commenting on the above report the "*Lancet*" (L.i./II,1024) says—steps taken by other countries, *e.g.*, Australia, U.S.A., and Switzerland, to banish by statute the practice of bleaching should be a useful object lesson to the legislators of this country. (Though not allowed for sale in the United States *there is nothing to prevent millers in U.S.A. from exporting bleached flour.*—L.ii./II,1045). The process cannot be viewed as free from risk to the consumer—especially in regard to the inhibitory effect on digestive processes and enzymes. Many millers are unaware of the nature and composition of the improvers they add. *The whole practice is conducted to make an inferior article attractive.*

B.M.J. i./II,881, also gives some very complete abstracts of these Reports. The commercial aspect has a humorous side as is shown by the following:—

'Some millers are at present only deterred from installing bleaching plants by consideration of expense. Others have had plants installed but have discontinued using them, in some cases for the reason that they were unwilling to pay the patentees for permission to use the process.' There is a possibility that the anti-bleach agitation may have been initiated by an interested miller.

The Local Government Board issued a further report on "The Nature of the Colouring-matter of Flour and its Relation to Processes of Natural and Artificial Bleaching." G. W. Monier-Williams shows herein that the colouring-matter is either carotene or a substance closely allied to it. The colour of this body is discharged by oxygen or by nitrogen peroxide. On exposure to the air it is bleached by absorption of oxygen, no oxides of nitrogen being absorbed, and it is reasonable to assume that the natural ageing of flour is a similar process, while in the bleaching of flour by nitrogen peroxide substances are produced which are not produced during the natural ageing of flour. Unbleached flour contains some nitrite reacting substance, but this is equivalent to not more than 1.5 to 2 parts of sodium nitrite per million; the effect



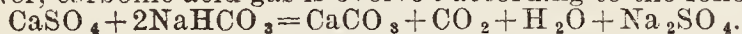
of excessive bleaching on the baking qualities of flour is dealt with. As much as 158 parts of sodium nitrite may be present in a million parts of bleached flour which contained 0.5 parts before bleaching, and that bread made from it contained 75 parts sodium nitrite per mill. The report contains spectroscopic diagrams illustrating detection of colouring matter and the effect of bleaching upon it. —C.D. ii./12,751.

A reply to the anti-bleach proposition states that Nitrites do not interfere with the action of diastase on starch, also that pancreatic digestion is not inhibited by relatively large quantities of Nitrites. Further, that direct experiments with the compound of the colouring matter of the flour with oxides of nitrogen showed that this is not poisonous nor does it have any perceptible action on the blood.—J.C.S.I., Jan., 1912, p. 40.

### Calcium Sulphate in Baking Powder and Self-raising Flour.

Baking Powders, according to a L.G.B. Report on 'the presence of Calcium Sulphate in Baking Powder and Self-raising flour' (Food Report No. 13, 1911 by Dr. Hamill,) in use in this country are conveniently classed into two groups (1)—this being far the larger—tartaric powders in which the acidic constituent is tartaric acid, cream of tartar, or a mixture of these, and (2) the phosphate powders, the acidic constituent of which is acid calcium phosphate together with sodium bicarbonate in all cases. Ammonium carbonate is extensively used *per se* as a necessary ingredient in the baking of sponge cakes and other light bread products. Alum is not now employed, although it is capable of acting as an acidic constituent, and was formerly much used. In an addendum by C. H. Cribb, regarding the use of phosphate baking powders and the alleged utility of calcium sulphate in them, it is stated:

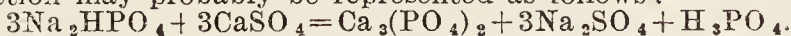
When calcium sulphate is mixed with sodium bicarbonate in the presence of water, carbonic acid gas is evolved according to the following equation:



The evolution of gas commences immediately, but is very slow, so that at the end of  $\frac{1}{2}$  an hour only 59 per cent. and after one hour 79 per cent. of the theoretical quantity was found to have been liberated, and even after three hours the reaction was not complete. When acid calcium phosphate acts upon sodium bicarbonate one of the products of the reaction is hydrogen disodium phosphate thus:



and this salt in turn reacts under suitable conditions with calcium sulphate, giving rise to phosphoric acid, which in turn can liberate a fresh quantity of carbon dioxide from any carbonate which may be present. The first part of the reaction may probably be represented as follows:



In actual baking experiments with a baking-powder containing calcium sulphate, 75 per cent. of the calcium sulphate was recovered unchanged from the finished loaf. Other experiments would seem to indicate that the calcium sulphate which has disappeared as such in the loaf is again re-formed by the agency of the acid in the gastric juice when the bread is eaten.

Calcium Sulphate occurs in commercial acid calcium phosphates to the extent of 2 or 3 per cent. up to 50 per cent. The proportion varies according to the method of preparing the calcium phosphate.

It is generally made from bone ash by means of phosphoric and sulphuric acid. When commercial phosphoric acid only is added to

the bone ash, a product can be obtained containing as little as 2 per cent. or as much as 9 per cent. of calcium sulphate. When sulphuric acid alone is used, the product may contain as much as 50 per cent. of calcium sulphate; mixtures of these acids give values intermediate between the extremes mentioned. It is also stated that calcium sulphate is sometimes deliberately added as a diluent. In order to keep the acid phosphate and sodium bicarbonate from too intimate contact, a neutral non-hygroscopic powder, known as 'filling,' is added, such as corn flour or rice flour, the last-named being generally preferred. The filling commonly forms about one-half of the baking powder, but in cheaper powders this is exceeded. The following recipes are given in the report :

Calcium Acid Phosphate .. ..	50	..	37	..	2	..	77
Sodium Bicarbonate .. ..	25	..	23	..	1	..	41
Maize Starch, rice-flour or ground							

rice .. ..	25	..	40	..	3 to 10	..	50 to 100
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From  $\frac{1}{2}$  oz. to 1 oz. of baking powder is employed for each pound of flour, hence if the calcium acid phosphate of the first powder contained 50 per cent. of calcium sulphate,  $\frac{1}{2}$  ounce of the powder would contribute over 50 grains of calcium sulphate to the flour. The same remarks apply in regard to the calcium sulphate introduced with the phosphate, 70 grains per lb. being contained in the above flour if the first ingredient is 50 per cent. phosphate. The phosphate baking powders are said not to keep well and are not found in retail trade so much as among confectioners and bakers, who mix the ingredients when required, and so avoid deterioration. Self-raising flours are made according to the following formula :

Calcium acid phosphate .. ..	6 lb.
Sodium bicarbonate .. ..	3 lb.
Flour .. ..	280 lb.

Dr. Hamil makes the following recommendations (*inter alia*) :

(a) *Manufacturers of acid phosphates* should not prepare even their cheapest qualities of acid phosphate, for sale as food ingredient, in such a way that it contains more than 10 per cent. of calcium sulphate.

(b) *Bakers, self-raising flour makers*, and others using acid phosphate in the preparation of food, should limit themselves to acid phosphate of high commercial quality—calcium sulphate not to exceed 10 per cent.—L.G.B. Report and Editorial comment C.D. i/II, Index Fo. 545.

### Added Mineral Substances.—

'Improvers' in form of Acid Potassium Phosphate, or Acid Calcium Phosphate or even Phosphoric Acid enables the miller to use a larger proportion of cheap wheats in blending, etc., and introduces more water into the bread. These improvers may be contaminated with Arsenic and in any case their addition is not in order. Flour contains its phosphorus in organic not inorganic form.—P.J. ii./ix, 71.

Section 3 of the Sale of Food and Drugs Act, 1875, provides that no person shall mix any article of food with any ingredient or material to render it injurious to health.—*c.f.* L i./12, 842.

Reverting again to the consideration of the best type of flour and bread made from it, Dr. Hamill in the No. 14 Food Report to the L.G.B. says in his *General Review*, the great practical difficulty in endeavouring to define any one variety of flour in terms of protein



content, mineral content or other criteria is that such a definition to be effective would require preliminary standardisation of wheat which is impracticable in view of the fact that wheat supplies vary from different parts of the world. It is evident that, unless we live wholly on bread, which is not desirable, the differences between one bread and another do not matter much.

With regard to choice of bread for children, however (though here also a varied diet is insisted on) it is stated—"For those children who live largely on bread—there appears to be advantage in bread from flour of the '*entire*' wheat class or from wholemeal in which the bran is very finely ground. In these the presence of the so-called offal, including the germ, secures a somewhat larger quantity of mineral matter and of suitably combined Phosphorus or other substances as yet unknown, which has been proved to be of importance.

Tankard expresses his opinion definitely in favour of *white bread*. He says that after reading the statements of well-known physiologists he is convinced that wholemeal bread, brown bread and bread made from 80% flour have no advantage. The crux of the matter seems to be that before the agitation a considerable quantity of inferior grades of wheat products could be readily obtained whereas subsequently little, if any of these products were to be had. The mineral constituents make, it is thought, no difference whatever as "our daily average food intake contains far more of such material than wanted for bone-forming, etc." (*Not so by any means in the case of the children of the poor.*—W. H. M.)

He suggests as standards not more than, say, 40% moisture, and that the bread shall be prepared from pure wheat flour unbleached and free from added mineral matter of any kind.

With regard to bran—it does contain a high proportion of mineral matter and of proteins but is of course excluded from white flour and also according to Tankard from the 80% flour;—in any case, the Nitrogenous constituents of the bran portion of the grain are, according to Tankard, thought to be practically non-digestible. So far as the germ of wheat is concerned this is rich in proteins, but it is doubtful how far these are, in the crude state, physiologically available to man.—P J. ii./11, 6, 71.

Jago (the '*Technology of Bread-making*'—1911, per P.J. ii./11, 436), points out that '*Standard*' Flour must include the germ of the wheat, but its enzymes give rise to objectionable changes from the very time of manufacture; excessive diastasic action is likely to occur with production of a sticky dough, and as a consequence heavy small loaves; acidity of the bread is also favoured as well as a tendency to the development of ropiness in the dough. As a set off to these objections there is the increased nutritive value of the bread.

CONCLUSIONS.—First of all the bleaching and '*improving*' of flours cannot be too strongly condemned. In our opinion the removal of the whole of the bran layer which contains so large a proportion of salts (see table), and which may be deemed "*bone-forming*" constituents, is an erroneous proceeding. Physiologists have not been able to agree on the subject—views are diametrically opposed. Extreme advocates on one side say the whole grain flour contains all the nutriment and that the white bread has nothing left in it, while the opponents of wholemeal bread appear to rely on the contention that '*offal*' and the parts of the grain until now given to swine, etc., are not digestible by human beings—especially delicate children.

Our own claims would be as follows :—

(1). *Wholemeal flour is undoubtedly of value to children and to all who digest it with ease. In such it cannot be proved to have injurious effect, on the contrary there is strong evidence that it is the more nutritive.*

(2). *Its more general use may be conducive to the more general exclusion of bleached and otherwise chemically treated flours of poor quality.*

(3). *The quality of ordinary white flour employed for bread making has latterly been deteriorating.*

### **NUX VOMICA (Off.).**

Now standardised to 1·25% Strychnine on the powdered drug (as U.S. *infra*).

Collection of Seeds in India, U.S. Consular report.—P.J. i./12,629.

Nux Vomica Oil, Unsaponifiable constituents of.—P.J. i./13,7.

Nux Vomica Seed, False, from Burmah, containing no Strychnine.—Plant not identified.—P.J. i./13,510,522.

#### **Assay Methods.**

U.S. standardises to 1·25% Strychnine. *U.S. Assay.* — Nux Vomica 20 Gm. in No. 60 powder is shaken with a mixture of Ether 137·5 Cc., Alcohol 13·5 Cc., Chloroform 44 Cc. and Ammonia 5 Cc., and allowed to stand 12 hours; 100 Cc. is decanted and shaken with repeated amounts of Normal Sulphuric Acid. Chloroform and Ammonia are added, and the mixture shaken and Chloroform drawn off. Chloroformic solution is evaporated and residue dissolved in warm Sulphuric Acid, and when cooled a cooled mixture of equal volumes Nitric Acid Sp. Gr. 1·42 (at 25° C.) and distilled water is added and the solution is shaken with Chloroform in the presence of excess of Soda. The Chloroformic solution is evaporated and the residue dissolved in N/10 Sulphuric Acid and back-titrated with N/50 Potassium Hydroxide in usual manner, using Iodeosin as indicator, the factor 0·0332 being employed to obtain percentage of Strychnine. (1 Cc. N/10 Acid = 0·03317 Gm. Strychnine.)

Bird's method modified for dry Extract.—P.J. ii./05,864.

A menstruum of Amyl Alcohol 1, Chloroform 3, and Ether 4 is a useful solvent for the alkaloids in assaying.—P.J. ii./00,574. A little Amyl Alcohol added to the Strychnine residue prevents decrepitation in drying.

Naylor favours a method based on Bird's or Alcock's process, concluding with Dowdard's Nitric Acid method of separating the two alkaloids.—P.J. ii./05,125. The fat of Nux Vomica is about 4%. For composition, vide P.J. ii./05,223.

The addition of 1 Cc. of 5% solution of Sodium Nitrite solution is suggested after dissolving the alkaloidal residue in 15 Cc. of 3% H<sub>2</sub>SO<sub>4</sub> and adding 3 Cc. of a mixture of nitric acid and water, in the U.S. process. To ensure the oxidation of the Brucine.—Am. Jl. Ph. 1907, p. 1, *et seq.*; Feb./08,74; or warm the strong acid with a few mgrs. of sugar until fumes appear, before diluting it.—A. B. Lyons, Int. Cong.

By using Nitric Acid Sp. Gr. 1·435 containing 1% Nitrogen peroxide, the Brucine is destroyed in a mixture of the alkaloids in 15 minutes.

In the estimation of Strychnine in presence of Brucine, D. B. Dott finds the Nitric Acid (Gordin's process) should be allowed to re-act at ordinary temperature for 20 minutes, and higher temperature should be avoided.—B.P. Conf., 1914; P.J. ii./14,120.

Alkaloidal strength of powdered drug to be 2·5%—F.I. Standardisation for total alkaloid does not limit the content of strychnine.

### **Extractum Nucis Vomicae Liquidum (Off.).**

*Off.*—Standardised to 1·5% Strychnine.

The U.S. process can be used for estimation, but there is no need to evaporate the alcohol from the fluid extract taken. Shake out 5 or 10 Cc. of same direct with an immiscible solvent in presence of alkali.—Am. Ph. Jl. 1906, 457. The brucine is entirely destroyed by the nitric acid in ten minutes if the solution is heated to 50° C.—this temperature is now employed. *Off.*

*Toxicology.*—Simplified method of extraction of Strychnine by means of Acetic Acid and Alcohol. The Alcohol is useful to assist filtration.—P.J. ii./07,639.



**Spectrum of Strychnine.**—The smallest quantity, *e.g.*, 1/500 grain, can be detected—useful in cases of poisoning. Alkaloids generally give characteristic spectra.—J. J. Dobble. Roy. Instn. Lecture, L. i./13, 1399.

## OLEA ESSENTIALIA.

**“The History and Chemical Relations of the Terpenes.”**—One of a series of Post Graduate Lectures at the Pharm. Soc., by Sir W. A. Tilden, complete report, *Perfumery Record*, July 9, 1912.

Synthesis of the Terpenes.—Prof. Perkin, *ibid.*

Essential Oils,—their constitution and commerce.—J. C. Umney, *ibid.*

For cold **enfleurage** as used for Jasmin and Tuberose, a mixture of pork and beef fat is used.

**Warm enfleurage** can be used for the more stable Essential Oils, *e.g.*, Rose, Cassia and Violet.

Petroleum Ether is also largely used, *e.g.*, for Violet. On removal of the solvent the so-called **concretes** are obtained, *i.e.*, oils + resins, fats, colouring matter, etc.,—these by-products have to be removed to produce the “**Absolutes**.”—J. C. Umney, P.R., July, 1912.

For the extraction of perfumes by distillation, solvent, etc., methods in addition to the above.—See P.R., Dec. 1913, 414.

**Sources of Various Oils.**—Island of Reunion yields Geranium Oil, Mexico.—Linaloe Oil. French Guiana.—Bois de Rose Femelle (for producing lily of the valley odours). Philippine Islands and Madagascar.—Ylang Ylang. Java, Burmah and Uganda.—Citronella Oils.

This latter oil is now used for making various artificial violet bodies.—J. C. Umney, P.R. Dec. 1913, 414.

**Saponification process** for Esters in Essential Oils and **Acetylation process** for alcoholic constituents are now given in B.P. Appendix, *c.f.* our Edn. XV., Vol. II., p. 58.

See also Essential Oils.—C.D. i./10, 63, 77, 94, 117, 151, 178, 304, 341. Refractive Index of Essential and Fixed Oils.—C.D. i./10 50.

## **Terpeneless and Sesquiterpeneless (‘T. and S. Free’) Essential Oils.**

Essential Oils, deprived of their Terpenes and Sesquiterpenes, which in many instances constitute a large proportion of the Oils have the advantage of being *stronger in flavour and perfume* than the natural Oils and are much more readily *soluble* than the latter.

*Note*—The Terpene- and Sesquiterpene- Free Oils are obviously more concentrated than the Terpene Free Oils. For example, it is claimed that 70 and 80 of Terpene- and Sesquiterpene free Lemon Oil=100 of the Terpene-free Oil and that 50 to 60 of ‘T. & S. free’ Pumilio Pine Oil=100 of the ‘T free’ Oil.

We have arranged a table of Solubilities showing the quantities of the ‘T. & S. free’ Oils which will dissolve in specified amounts of weak Spirit—45, 60 and 70 % Spirits have been selected as probably generally useful. This table is based on data supplied by Sachsse & Co. It has been rearranged to suit English pharmacists’ requirements.

## TERPENE AND SESQUITERPENELESS OILS.

'T and S free' Oil.	Equivalent to 100 of Natural Oil.	Solubility in Alcohol.		
		100 Gm (112·38 Cc) of 70% (by vol.)	100 Gm (109·47 Cc) of 60% (by vol.)	100 Gm (106 Cc) of 45% (by vol.)
		Gm.	Gm.	Gm.
Caraway .. ..	50	50	20	2
Cinnamon (Ceylon) ..	75	35	3	0·175
Clove (Buds) .. ..	75	60	30	0·25
Coriander .. ..	75	50	15	0·35
Cumin .. ..	30	7·5	0·5	1*
Dill .. ..	40	70	15	0·5†
Eucalyptus Globulus .	75	75	12	0·3†
Fennel.. ..	35	2·7	0·8	0·6†
Geranium Afric. ..	75	70	10	0·18
Geranium French ..	75	70	2·5	0·1
Lavender .. ..	70	40	3·5	0·1
Lemon.. ..	3·5	50	5	0·25
Lemongrass .. ..	75	40	3·5	0·1
Limetta .. ..	8	70	20	0·15
Marjoram .. ..	35	5	1	1·5*
Myrtle.. ..	30	30	10	0·25
Neroli .. ..	40	30	2	0·12
Nutmeg .. ..	15	2·5	0·5	0·4*
Opoponax .. ..	20	4	0·4	0·35*
Orange, Bitter ..	1·7	25	1·5	0·9*
Orange, Sweet ..	1·75	40	1·7	0·1
Parsley .. ..	70	3·5	1·5	2*
Peppermint(American)	75	20	1	1*
„ Jap. ..	75	30	2·5	0·15
„ Mitcham ..	75	30	7	0·2
Pimento .. ..	75	50	2	0·1
Pinus Pumilio ..	6·6	0·3	0·1	0·25†
Pinus Siberica ..	35	25	2·5	0·1
Pinus Sylvestris ..	15	40	1·5	1·5*
Rosemary .. ..	30	70	18	0·5
Rose, Bulgarian ..	75	0·25	0·12	0·15*
Sandal Wood . ..	80	10	2·5	0·8*
Spearmint .. ..	70	35	1	0·6*
Star Anise .. ..	75	2·7	0·8	0·6†
Thyme.. ..	25	25	8	0·1*

*Note.*— \*These figures refer to weights of a 1 in 10 solution in Alcohol 80% by volume.

† These refer to weights of a 1 in 10 solution in Alcohol 90% by volume. *All other figures refer to the actual Terpene- and Sesquiterpene-free-Oils.*



It is doubtful whether an oil containing very delicate esters, *e.g.*, **Bergamot Oil**, is improved by removing the terpenes. Further, there is no point whatever in rendering terpeneless an oil consisting almost entirely of its odorous constituent such as **Clove Oil**.

**Lemon Oils** from which the terpenes only have been removed contain in the neighbourhood of 42 to 45% Citral, whilst those from which the sesquiterpenes have also been taken contain up to 65%, or, as claimed by some makers, 72% Citral. The removal of the sesquiterpenes, in addition to the terpenes, causes the Oil to lose the sweetness and softness of a well-made terpeneless oil. Some users hold that the best results are obtained with an Oil containing under 40% Citral from which the whole of the terpenes have not been removed.—E. J. Parry, C.D. ii./13,378.

**Synthetic Perfumes.**—For a synopsis of the principal bodies used in making synthetic perfumes *vide* Pharm. Formulas, 1914, and Perfumery Record, July 5, 1914.

### ANTISEPTIC POWERS OF ESSENTIAL OILS.

We took occasion in 1910 to determine the "*Lancet*" Carbolic Acid Coefficient (using *B. Coli Communis*) of the more important Essential Oils and aromatic substances.

The experiments were conducted with selected Oils of known composition.

The paper in question, *vide* "Perfumery and Essential Oil Record," Nov., 1910, was divided into two portions—the first giving the minimum lethal strengths, using Aqueous Solutions with 2 and 30 minutes contact, and the second the minimum lethal strengths with Saponaceous Solutions (diluted at time of use to form emulsions). From these the **Carbolic Coefficients** were obtained by stating the comparative strength with Phenol Solution. In other words by dividing the M.L.S. (Minimum Lethal Strength) as compared with unity of the Essential Oil Dilutions by the M.L.S. as compared with unity of the *Phenol* Dilution, we obtained Coefficient figures at respectively 2 and 30 minutes—(100 and 170 respectively were the M.L.S. for Phenol)—the mean of the two results is the Carbolic Acid Coefficient.

The antiseptic power of many of the Oils cannot be determined by Aqueous solution owing to the fact that a saturated aqueous solution is not strong enough to kill the test organism—here the Saponaceous Solutions overcome the difficulty.

The Coefficients so obtained show that several of the Oils possess considerable antiseptic power. It is of interest to note that the two isomeric monatomic phenols, Carvacrol and Thymol, homologues of Phenol (acknowledged valuable antiseptics)—disputing the premier position in the table, have almost the highest molecular weights of those occurring in the commoner Essential Oils.

It must be clearly understood that the Coefficients are merely approximate. Further it is obvious that these Oils might produce entirely different Coefficients if another organism were employed. The Eucalyptus Oils and Eucalyptol for example, might appear higher in the scale if the organisms associated with nasal catarrh, *e.g.*, *B. Septus*, *B. Influenzae*, *B. Friedländer*, *Pneumococcus*, *M. paratetragenus* or *M. Catarrhalis*, etc.—were used as test organisms.

The details of methods employed are given in the original paper. Several criticisms of the paper which appeared are now replied to.

As an outcome of this investigation Saponaceous Solutions of some of the Essential Oils are prepared for physicians' use under the name—

### Perfumed Formosyls, *vide* Vol. I.

The results were briefly as follows :—

Essential Oil Dilution.	C.A.Co-efft	Chief Chemical Constituents.
<i>Origanum</i> Oil (A.) .. ..	26	82% Phenols, <i>e.g.</i> , Carvacrol.
<i>Thymol</i> (S).. ..	25	—
<i>Carvacrol</i> (S) .. ..	21	—
<i>Thymol</i> (A.) .. ..	19	—
<i>Thyme</i> Oil (S.) .. ..	15	46% Phenols (Thymol, &c.)
<i>Thyme</i> Oil (A.) .. ..	13	<i>As above.</i>
<i>Geraniol</i> (S.) .. ..	12	—
<i>Cinnamon Leaf</i> Oil (S.) ..	10	86% Phenols, <i>e.g.</i> , Eugenol.
<i>Cinnamon Bark</i> Oil (S.) ..	9	52% Aldehyde <i>e.g.</i> , Cinnamic.
<i>Cloves</i> Oil (S.) .. ..	9	90% Phenols, <i>e.g.</i> , Eugenol <i>v. ante.</i>
<i>Cinnamic Aldehyde</i> (S) ..	8	—
<i>Citronellol</i> (S.) .. ..	8	—
<i>Cinnamon Bark</i> Oil (S.) ..	8	82% Aldehyde (Cinnamic Aldehyde)
<i>Cinnamon Bark</i> Oil (A.) ..	7	82% Aldehyde.
<i>Rosemary</i> Oil (S) .. ..	6	—
<i>Otto of Rose</i> (S.) .. ..	6	68% alcohols estimated as Geraniol.
<i>Cassia</i> Oil (S.) .. ..	5	83.5% Aldehyde (Cinnamic).
<i>Wintergreen</i> Oil (S.) ..	5	Methyl Salicylate.
<i>Eucalyptus Amygd.</i> (S.) ..	5	Chiefly Phellandrene (a Terpene) and Eucalyptol.
<i>Lavender</i> Oil ( <i>English</i> ) (S)	5	Esters as Linalyl Acetate $\text{CH}_3\text{COOC}_{11}\text{H}_{17}$ , 11%. Linalool is isomeric with Geraniol. Other constituents of the oil are Linalool as such, Esters, other than the Acetate, Cineol and Limonene.
<i>Limon</i> Oil (S.) .. ..	4	Limonene, Citral 4 to 7% Citronellal, Geranyl Acetate, possibly other esters of Geraniol and Citronellal.
<i>Almond</i> Oil, <i>Essential</i> , S.A.P (S.) .. ..	4	Benzaldehyde chiefly.
<i>Eucalyptol</i> (S.) .. ..	4	—
<i>Eucalypt. Glob. Oil</i> (S) ..	4	67% Eucalyptol together with Pinene, Phellandrene, Alcohols and Aldehydes
<i>Garlic</i> Oil .. ..	2	Allyl Sulphide chiefly, see p. 195.
<i>Light Oil of Tar</i> ( <i>Rectified</i> ) (S) .. ..	2	Volatile Bodies. Contains no Phenols.
<i>Santal</i> Oil (S) .. ..	1½	Contains 93.8% Alcohol calculated as Santalol $\text{C}_{15}\text{H}_{23}\text{OH}$ .
<i>Birch Tar</i> Oil (S) .. ..	1½	Stated to contain Guaiacol, Cresol and Pyrocatechin.
<i>Cade</i> Oil (S) .. ..	1	—

A = Aqueous Solution.

S = Saponaceous Solution.



## REPLIES TO CRITICISMS.

B.M.J. ii./10,1935, enquired for details of manufacture of the Saponaceous Solutions used and pointed out that Emulsions of different Oils may vary. The figures are also criticised and the fact that Eucalyptus and Sandal Wood Oil appear so low is remarked upon.—In reply we would say that the Saponaceous Solutions were pharmaceutically prepared and from these, Emulsions were produced with water.

In respect to **Eucalyptus** and **Santal Oils**, these surely have a claim to be classed as powerful germicides seeing we find they are 4 and  $1\frac{1}{2}$  times, respectively, as powerful as Carbolic Acid, which itself ranks as a strong disinfectant. The surprise is that they should approach the power of Phenol at all, especially Santal Oil, which is a bland innocuous substance compared with Phenol.

We agree as to the general belief that the physical conditions of such emulsions may be of importance. In support of this it is frequently pointed out in the paper that the soap present appears to assist in germicidal power, possibly by mechanical action.

We cannot agree that comparative results with Oils differ to such an extent that Emulsions of Essential Oils (made as nearly as circumstances will permit under identical conditions) may be no criterion as to relative antiseptic powers. The results give the relative strengths of certain Oils under stated conditions. Since this criticism appeared we determined very approximately with the aid of a Thoma Zeiss apparatus the size of the globules of the Oils in the Emulsion all of dilution strength 1 in 120 and found as follows:—

Gaultheria Oil	..	..	..	..	$\frac{1}{2}$ to 5 microns.
Cinnamon Bark Oil (82% Aldehyde)	..	..	..	..	1, 10 "
Cassia Oil	..	..	..	..	1, 10 "
Sandal Wood Oil	..	..	..	..	$\frac{1}{2}$ " 5 "
Lemon Oil	..	..	..	..	$\frac{1}{2}$ " 2 "
Eucalyptus Amygdalina Oil	..	..	..	..	$\frac{1}{2}$ " 2 "
Origanum Oil	..	..	..	..	$\frac{1}{2}$ " 5 "
Rosemary Oil	..	..	..	..	$\frac{1}{2}$ " 5 "
Tar Oil	..	..	..	..	$\frac{1}{2}$ " 2 "
Lavender Oil	..	..	..	..	Nil.
Eucalyptol	..	..	..	..	Nil.
Eucalyptus Globulus Oil	..	..	..	..	Nil.

The minimum lethal strengths of the various Oils were in most instances less than this 1 in 120; this strength was found convenient to work with in the Thoma Zeiss cell. The size of the globules operating on the bacilli in the experiments may therefore be taken as certainly not larger than the dimensions stated above. It may be of interest to note that the diameter of the fat globules in cows' milk is on an average  $1\frac{1}{2}$  to 10 microns, hence our Emulsions may be regarded as satisfactory. The length of the Colon Bacillus is about 2 to 4 microns.

Clearly the smaller the dimensions of the globules the greater number of them present and the larger the surface area of the chemical substances to act upon the bacteria. We deal with the chemical action later.

With regard to figures our B.M.J. critic draws attention to the fact that we obtained a Coefficient for Origanum Oil containing 82% Carvacrol of 25.8 whilst Carvacrol as such only showed a coefficient of 21.3. It is obvious that the constituents making up the balance of 18% of the Oil may have chemically or physically greater potency than Carvacrol itself, or they may enhance the activity of Carvacrol. The difference between the Minimum Lethal Strengths as at 2 and 30 minutes, which gave the Coefficients 21.3 and 25.8 is practically negligible when one recalls the fact that we are dealing with a minute bacillus and an antiseptic under empirical conditions. For further data in answer see "Perfumery Record," Jan., 1911.

With regard to the "Lancet" criticism (Lancet, Dec. 11, 1910, p. 1779) we would refer to the remarks above as to the size of the globules. The "Lancet" says:—

"The relative values of the Oils in regard to Carbolic efficiency may not necessarily be dependent upon the essential constituent, for undoubtedly a greater inhibitory action on organisms is shown by a perfectly uniform emulsion, in which the separated particles are exceedingly fine, than by an emulsion which exhibits irregularities or suspended particles varying in dimensions." The matter might, therefore develop into the question, What is a uniform

Emulsion, and what diameter shall the oil globules have? If cows' milk be regarded as a uniform emulsion then the Emulsions produced by our Saponaceous Solutions according to our measurements may come within this category.

The "*Lancet*" remarks that Surgeons and Physicians "are not necessarily dependent upon disagreeably smelling Phenol compounds as the basis of strong germicidal preparations."

With regard to the "*Chemist and Druggist's*" remarks, the fact that the efficacy of Eucalyptus Oils in colds and catarrhs is 'not owing to bactericidal properties as measured on *B. Coli Communis*' is evident from the figures. It is quite likely that any kind of Eucalyptus Oil kills the influenza and catarrhal bacilli better than most other essential oils. Experiments which we instituted with certain catarrhal organisms had to be reluctantly dropped for the reason that we found the organisms difficult to cultivate in the conditions required—it was impossible to draw conclusions from the results.

*A well-defined, easily-cultivated bacterium is absolutely essential for such experiments.*

'*The Lancet*' (L. ii./12,1387) in a review of the action of Phenols and other bodies on bacterial protein which gives them marked bactericidal action, enquires as to how the Essential Oils act. What affinity, if any, occurs between the oils and bacterial protein?

It is shown that certain substances, *e.g.*, Formaldehyde, have a direct interacting power with Protein. In the case of the Phenols and Cresols the action is more complex and a theory has been set up on the lines of an upheaval of the colloidal elements of the bacterial body and consequent formation of an irreversible substance. The precipitated protein is not again dispersed. The action is in short very similar to that of heat—as in the case of heating egg albumen.

Bringing this to bear upon the Essential Oils we see that the Oil heading the list contains 82% of Carvacrol or allied Phenol and that the substance is practically as strong as is the phenolic Thymol which is isomeric with it. Then follows Thyme Oil with 46% Thymol and subsequently Cinnamon Leaf and Clove Oil containing 86% to 90% Eugenol (or allied bodies). A little lower comes Cinnamon Bark Oil (82% Aldehyde).

In short we have in these preparations, *especially in the minute subdivision effected in Saponaceous Emulsions just the very bodies—higher up in the homologous series* which were known to be markedly antiseptic. The two isomeric PHENOLS which rank highest in our experiments have almost the highest molecular weights of those occurring in the commoner Essential Oils—far higher than Phenol or the Cresols, herein is doubtless an answer to the question of how the Essential Oils act. To introduce the colloidal theories would not appear to greatly assist the matter. We should ascribe the effect to one analogous with that of the caustic action of Phenol on the tissues—a direct attack on protein. Bacterial protein one assumes to be particularly responsive to these antiseptic oils.

Geinitz—Schimmel's Report, October, 1912—has made some comparative experiments on the narcotic and disinfecting action of Essential Oils. The two do not correspond. Anise, *e.g.*, and its constituent Anethol have no antiseptic action, but both are strongly narcotic to fish (roach were used). Amongst the strongly narcotic oils were:—

Mustard Oil—limit dilution .. ..	1 to 1,320,000.
Cinnamon .. ..	1 to 180,000.
Citral .. ..	1 to 153,846.
Carvacrol .. ..	1 to 134,010.
Anethol , .. ..	1 to 104,587.



The antiseptic power was determined by mixing 10 Cc. of fresh milk with a knife-point of sulphur and afterwards adding the Antiseptic. Hydrogen Sulphide evolution (by bacterial action) was tested for with lead paper on the top of the tubes. Amongst the results were:—

Mustard Oil—limit dilution .. ..	1 to 2 697.
Cinnamon Oil „ „ .. ..	1 to 987.
Anisic Aldehyde „ „ .. ..	1 to 170.
Phenol „ „ .. ..	1 to 160.
Carvacrol „ „ .. ..	1 to 111.
Clove Oil „ „ .. ..	1 to 75.
Thyme Oil „ „ .. ..	1 to 32.
Lavender Oil „ „ .. ..	1 to 29.

The results are of interest, though not comparable with our own work, using a single definite organism—*B. Coli*. Geinitz's results clearly cannot be regarded as of great accuracy.

Essential Oils, Preservative action—estimated roughly by their power of preventing growth of mould in a 50% Glucose and a 50% Sugar Solution containing Meat Extract. Of those that did *not* act as preservatives may be cited,—Calamus, Celery, Cubeb, Lemon, Orange Peel, Sandal. The list of those with preservative action resembles our own earlier findings, *c.f. antea*. To these may be added Cajuput, Cardamom, Chenopodium and Cumin.—*J. Amer. Pharm. Ass.* 1912, 1, 1273; *P.J.* ii./12, 649; *Y.B.P.* 1913, 79.

SOLUBILITY OF WATER IN ESSENTIAL OILS.—The “Terpene” group of Oils Nutmeg, Juniper, Lemon and Orange, etc., is incapable of dissolving water to any extent.—*P.R.* Dec. 1912.

Essential Oils, Unification of Process of Analysis.—Umney and Parry also Jeancard.—*P.R.* 1912, 245.

## OLEUM LAVANDULÆ FLORUM.

Volatile oil from *Lavandula vera* (*Labiatae*), (*L. officinalis* U.S.) has Sp. Gr. usually not below 0·885 up to 0·900 at 15·5° C. Soluble in three parts of 70% Alcohol. Shaken with water in a narrow graduated cylinder, volume of oil should not be diminished (absence of alcohol) (U.S.). French Oil never found higher than 44% in natural esters.—*C.D.* ii./09, 580. Terpinolene (*q.v.*) is an adulterant. It has been advised that the English oil should contain from 7 to 11% of esters, and the foreign oil not less than 30% of esters, calculated as linalyl acetate  $C_{10}H_{17}C_2H_3O_2 = 196·16$  I. Wts., as determined by saponification with alcoholic potash—this is now adopted, *Off*.

This 30% minimum for the foreign excludes some genuine high-grade samples.—Parry. There is no evidence to show that the esters improve the odour or that they have any medicinal value.—Henderson, *P.J.* ii./10, 138.

Ph. Ital. requires about 35% Linalyl Acetate.

## OLEUM LIMONIS.

*Syn.* Oleum Citri. P.G.V.

From fresh Lemon Peel by expression. Sp. Gr. 0·857 to 0·860. O.R. not less than + 59°. U.S. requires 4% Aldehyde by weight calculated as Citral. It ranges from 4 to 7%. Citral  $C_{10}H_{16}O = 152·128$  I. Wts. is optically inactive. Sp. Gr. 0·893 to 0·897. It occurs in a number of other essential oils. A somewhat extensive investigation by U.S.A. authorities went to show that where pinene is found in Lemon Oil, using ordinary means of distillation, it is *prima facie* evidence of adulteration.—Examination of Nitrosochloride crystals from the Oils.—*C.D.* ii./09, 824. Other authorities are, however, of opinion that Pinene is a natural constituent of Lemon Oil. Umney says Pinene may or may not be present. The Nitrosochlorides of other terpenes may be similar to that of pinene.

Bennett's Hydroxylamine process, *vide* *P.J.* i./09, 463. It appears to give results about 10% too low.—*P.J.* ii./10, 437.

P.G.V. requires that the oil shall be soluble clearly 1 in 12 of Alcohol—or to show only a little flocculent matter, *absence of Fatty Oil and Paraffin*.

Lemon Oil, Terpeneless and Sesquiterpeneless.—1 part equals in flavour 20 to 30 of ordinary Oil. It is soluble in comparatively weak Alcohol, see also *Olea Essentialia*, p. 100.

TERPENELESS LEMON OIL MANUFACTURE.

The distillation in Southern Italy is a very “rule of thumb” matter, and is as follows:

Lemon Oil of undoubted purity and good quality [*i.e.*, Citral (by  $\text{NH}_2\text{OH}$  method) 4·7 to 5% ; O.R. 60 to 64° at 15·5 ; Sp. Gr. 0·8570] is distilled in a copper still under reduced pressure—about 20 mm., at which it boils at 56 to 63°—a water bath is used. From this about 93% is distilled off consisting chiefly of Limonene containing 1·5 to 2·0% Citral ( $\text{NH}_2\text{OH}$  method). The residue in the still is now steam distilled and thus about 4½% “Terpeneless Oil” is obtained and about 2½ to 3% gummy residue left in the still. The Terpeneless Oil so obtained has O.R. of from—7 to—10° and a Citral content of from 35 to 40% ; Sp. Gr. 0·896 to 0·9. There are a few trade secrets connected with the matter. Oil which contains any impurity whatever is quite useless for the process. Turpentine (a favourite old adulterant) ruins the finished oil ; Terpenes diminish the quantity of product sought ; Lemon Grass Citral increases its quantity but gives it a “verbena” odour which would at once be detected by an expert. The Oil must be pressed from fruit which has been gathered by hand at the end of the “green” stage and just when it has become completely yellow ; the fruits must not be damaged.—W. C. Slater. For further details consult the works of Parry Allen, *etc.*

For Lemon Tincture and Syrup, *see Vol. I*, p.p. 829, 830.

‘**Oleum Citron**,’ so called, in this country is usually a blend of Lemon, Orange, *etc.* (Distinguish from *Oleum Citri*—“Citronenöl” P.G.V. which is our *Oleum Limonis*—*vide antea*). **Bergamot Oil** is from *Citrus bergamia* peel, by expression from the ordinary Bergamot. Sp. Gr. 0·882 to 0·888.

### OLEUM MENTHÆ PIPERITÆ.

Finest English white Mint Oils contain 12 to 15% esters, whilst the black variety rarely contains more than 8%.—P.J. ii./o8,624.

Analysis shows English Oils have a certain proportion of ester with a decidedly high pungency value as shown by the total menthol percentage, while French Oils are in the other extreme, *i.e.*, a low total Menthol with a somewhat high ester percentage. A blend of the two might be of use where pungency and softness is required.—P.J. ii./10,723,731.

Peppermint grown in a damp situation is said to yield only ¼ the amount of oil of that grown under ordinary conditions, but this is not the case in experiments at Hitchin. Cultivation in the shade does not appear to increase yield of oil.—*Vide* P.J. ii./11,175.

P.R. Year Book, 1913, gives following under “**Constants for Normal Essential Oils.**”

*English*—variety not stated—Sp. Gr. 0·900—0·910, total Menthol 55—65%, esters 3—15%.

*American*—Sp. Gr. 0·900—0·920, total Menthol 50—65%, esters 6—10%.

*Japanese*—Sp. Gr. 0·900—0·910, total Menthol 70—90%, esters 3—6%.

*Japanese Dimentholised*—Sp. Gr. 0·895—0·905, total Menthol 45—60%, esters 5—12%.

Evans’ Analytical Notes, 1913, gives :—

*English*—Sp. Gr. 0·905—0·907, total Menthol 59·2 to 65·7%, Menthyl Acetate 7·1 —8·6%.

*American*—Sp. Gr. 0·904—0·9075, total Menthol 55·4—65·0%. Menthyl Acetate 5·0—10·8%.

*Japanese Dimentholised*—Sp. Gr. 0·8985—0·9035, total Menthyl Acetate 7·8—8·1%.

*Rectified Oils*—Sp. Gr. 0·9005—0·904, total Menthol 56·1—60·6%, Menthyl Acetate 8·8—11·7%.

*Off.* requires not less than 50% Menthol and 5% Esters calculated as Menthyl Acetate.

**Menthol and Peppermint Oil in Alcohol Solution.—Test to distinguish.**

If Tincture of Iodine be added to a Solution of Peppermint Oil, several drops, more or less, may be added before the yellow tint of Iodine is perceptible. With a solution of Menthol there is no absorption, so the yellow tint is seen at once.—Y.B.P. 1913,88.

### OLEUM MORRHUÆ. (*Off.*).

Sp. Gr. 0·924—0·931 includes all genuine samples. **Unsaponifiable Matter.** In good quality oil rarely exceeds 1·6% ; use full excess of alkali before extraction ; wash Ethereal Extract at least 4 times (Parry). **Free Fatty**



Acid calculated as Oleic should not exceed 1%, easily estimated. Many samples fall below 0.5%. Iodine Number 155 to 170 (Hübl's Solution ditto). We found Acid Value not exceeding 2.5. No separation of solid fat should take place on exposure of the oil to a temperature of 0° C. for three hours. (*Off.*). 1 Cc. of the oil dissolved in 10 Cc. of Carbon Disulphide may give a violet blue colouration when gently shaken with one drop of Sulphuric Acid.

An authentic sample of Norwegian Oil gave Sp. Gr. 0.9270, S.V. 185.8, I.V. 165.2. Unsaponifiable matter 0.69%,  $\eta_{sp}$  1.4800, free fatty acid (as Oleic) 0.32%.—Southall's Rep. 1913, p. 10, per Y.B.P. 1913, 100.

Bases to the extent of 0.05% have been found, including Butylamine, Isoamylamine, Hexylamine, Dihydrolutidine, which are volatile and the non-volatile Morrhaine  $C_{19}H_{27}N_3$  and Aselline  $C_{25}H_{32}N_4$ . Fahrion assumed the presence of Asellic Acid  $C_{17}H_{32}O_2$  in the liquid fatty acids from Cod Liver Oil, which had I.V. 175.5. Cholesterol is a characteristic constituent ranging from 0.46 to 1.3%.—Benedict and Lewkowitsch, p. 392.

Phosphorus, it is said, is not found in neutral oils, but only in acid samples and Iodine only when decomposition of the liver has occurred. This indicates that the activity of the oil is not due to these bodies. Presence of the last-mentioned may be sought by fusing with Sodium Carbonate.

I.V.'s (by Wij's method) 118.4—178.7 were found for the oil and 165.6—178.7 for the Acids obtained therefrom, indicating molecular values 319.7—524.4. Hydroxylation and polymerisation between the double bonds and Carboxyl groups may possibly account for a decrease in I.V. In an attempt to prepare the Acids as they exist in the oil, *e.g.*, by treating with Alcoholic Potash in presence of Hydrogen, an acid with 18 carbons and 4 double bonds, having a molecular weight of 290.5 was obtained.—Owen T. Williams, P.J. ii./12, 806.

E. F. Harrison regards Iodine Monobromide as the most trustworthy reagent. He obtained I.V. 165—170 for the Oil. O. T. Williams stated he had subsequently obtained similar figures on other samples of oil.

For further details of the general chemical composition, see Vol. I., especially a paper by O. T. Williams, p.p. 559, 560. *c.f.* also Oleum Papaveris, Vol. I.

## OLEUM OLIVÆ (*Off.*).

Sp. Gr. 0.915 to 0.918. U.S. Saponification No. is 188 to 197 and Iodine No. not less than 80 or more than 88. *Off.* differs slightly in Iodine No.

The action of oxygen on the oil increases the Saponification No. and reduces the Iodine No.—Am. Jl. Ph. July, '07, 308.

Seven samples showed Iodine No. average 80.9, minimum 77.4, maximum 89.4.—Am. Jl. Ph., Apl. '12, 158.

2 Cc. of the Oil mixed with 1 Cc. of Amyl Alcohol and 1 Cc. of a 1% Solution of Sulphur in Carbon Disulphide and placed in a test tube immersed in boiling water should not develop a red colour in 15 minutes—absence of Cotton Seed Oil, *i.e.* Halphen's Test (Works better using boiling brine.—Southall's Lab. Rep. 1907.)

Renard's Test (Archbutt modification, detailed in 'Lewkowitsch.' 3rd Edn. Vol 2, p. 6) found satisfactory for detecting adulteration (Arachis Oil).—Southall Lab. Rep. 1912.

Test for Arachis Oil (U.S.). Boil 1 Cc. of the Oil and 15 Cc. of Alcoholic N

$\frac{1}{1}$  KOH for 20 minutes under reflux condenser and keep 24 hours at not exceeding 15° C. A cloudiness or distinct deposit of crystals (Potassium Arachidate) would indicate presence of Arachis Oil. The test can be modified to give quantitative results.—Bohrisch—Pharm. Zeit., 1910, 471.

Test for Sesame Oil.—2 Cc. of the Oil shaken for  $\frac{1}{2}$  minute with 1 Cc. of strong Hydrochloric Acid containing 1% of Cane Sugar and allowed to stand for 5 minutes, the acid layer should not become pink (U.S. slightly modified). Our experiments showed that 5% or even less of Sesame Oil working with a pure control is quite easily detected by this test. We found that 20% of Sesame Oil gives a deep red. The reagent must be freshly prepared.

It is also necessary that the Sesame Oil shall be recent. We have found that old Sesame Oil fails to give the red colour—on the contrary, it produces a characteristic light green colour.

**Nitric Acid Test** for other Oils.—Agitate 5 Cc. of the oil with 5 Cc. of  $\text{HNO}_3$ , Sp. Gr. 1.30 and heat for 5 minutes. There should be no darkening and the oil should have set firm in 12 to 18 hours.

### OLEUM ROSÆ.

**Characters and Tests.**—The Sp. Gr. of Otto ranges from about 0.850 to 0.860 at 30° C. (compared with water at 15° C.), R.I. at 25° about 1.460 to 1.465; M.Pt. about 20° to 22.5° C. Mixed with an equal volume of chloroform it does not congeal and is convenient for use. Saponification value (U.S.) not less than 10 nor more than 17. It contains 70 to 75% of

**Geraniol**  $\text{CH}_3 > \text{CH}-\text{CH}_2-\text{CH}=\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{OH}$  or  $\text{C}_{10}\text{H}_{18}\text{O}$  = 154.144 I. Wts. (three-quarters of the liquid portion), and **Citronellol**  $\text{C}_{10}\text{H}_{20}\text{O}$  = 156.16 I. Wts. (the remaining 25%). Linalool is isomeric with Geraniol, Sp. Gr. 0.870. B.Pt. 197°. It is contained in Coriander, Thyme and other oils and is either + or - rotatory.

*Off.* Constants for Sp. Gr., etc., of Otto differ from the above in some particulars.

In commerce '**Rhodinol**' is a blend of the two Alcohols from Pelargonium Leaf Oil. It is a mixture of Geraniol and Citronellol and not a pure substance. Some workers give the name as synonymous with Geraniol—others as synonymous with Citronellol.

75 or 76% at most is the highest amount of alcohol calculated as Geraniol that should be allowed in a normal pure Otto. Pure Otto never has specific gravity as high as 0.862. Frequently it is as low as 0.850. Any Otto with a refractive index below 1.4600 is adulterated, and almost invariably with alcohol. Considering that about 50% of the adulterated samples contain alcohol, which is used to adjust the high Sp. Gr. and R.I. of the Geraniol Compounds added, the following test (invariably applied by analysts) is valuable.

"If 5 Cc. be well shaken with 10 Cc. of warm water and the mixture allowed to separate, the refractive index of the washed oil at 25° C. should not differ from that of the original oil by more than 0.0015 (absence of alcohol)."

The determination of the R.I. should be made on the separated otto when quite clear, filtered if necessary, but not dried with any drying agent, since the original oil, owing to the method of distillation is saturated with water.—Parry C.D. ii./11,450.

Otto of Rose analysis and details of Adulterants,—Alcohol, Oleum Cedri Ligni, Palmarose, Gurjun Oil, etc.—P.R., Dec., 1913,416.

Though the predominating constituent, Geraniol is by no means the most important as both Citronellol and Nerol, and esters of the respective Alcohols and other bodies contribute largely to its fragrance. Phenyl Ethyl Alcohol, which possesses a mild odor, appears to be contained in Otto and in Neroli Oil, not only as such but also in form of esters of Benzoic and Phenyl Acetic Acids. Although this Alcohol is contained in exceedingly small quantity in Otto, it represents quantitatively the chief volatile constituent of rose petals. Being freely soluble in water, it remains behind for the most part in the aqueous portion of the distillate from which the Otto has been removed.

The so-called **Stearoptene** of Otto is a Paraffin with formula  $\text{C}_{16}\text{H}_{34}$ , but Schimmel showed recently that it is not a simple substance but a mixture of homologous hydrocarbons.—F. B. Power, P.J. ii./13,490; C.D. ii./13,515.

Geraniol and Citronellol estimation, Bouley's Method.—Bull. Soc. Chim. 1912,11,915; Y.B.P. 1913,73; Bennett P.R. 1913,3,334.

The presence of Otto in the air is readily recognised when only 0.000,000,000,000,333 Gm. of it is present in a cubic mm. of air.—L. i./13,184.

### OLEUM ROSMARINI.

A colourless or pale yellow oil soluble 1 in 1 of 90% Alcohol and 1 in 5 to 10 of 80% Alcohol. Distilled from flowering tops of *Rosmarinus Officinalis* (*Labiatae*) Sp. Gr. from about 0.895 to 0.920. U.S. requires not less than 2.5% Ester calculated as Bornyl Acetate and not less than 10% of Alcohols calculated as Borneol.—*Off.* requires practically all these constants.

Internally it is a carminative, and externally promotes the growth of the hair.



Optical rotation varies enormously. The oil distilled at Hitchin has been both + and - rotatory in different years. In 1905, 6 and 7 was  $-0^{\circ}24$  ;  $-0^{\circ}36'$  and  $-2^{\circ}48'$  respectively, temperature being  $20^{\circ}$  C.,  $20^{\circ}$  C. and  $14^{\circ}5'$  C. respectively. A pure oil is soluble in one-fourth its bulk of alcohol.—P.J. ii./07, 599.—P.J. ii./08, 624.

The suggested Rotation requirements (O.R.O $^{\circ}$  to  $+15^{\circ}$ ) exclude not only the 'Spanish (?)' Oils, but also the English. English Oil greatly superior in aroma. Further the Oil whether English or Foreign may be + or -. The English Oil Distillery should be encouraged.—P.J. ii./10, 140. O.R. actually adopted *Off.* is  $-2^{\circ}$  to  $+15^{\circ}$ .

### OLEUM SANTALI.

Sandal Wood Oil should be soluble 1 in 6 of 70% alcohol at  $20^{\circ}$  C. It should contain not less than 90% alcohols, calculated as santalol,  $C_{15}H_{24}O$ .—C.f. C.D. ii./09, 581; *vide* also P.J. ii./08, 624.

O.R. by general consensus of opinion should be lower than given in U.S. should be  $-12^{\circ}$  to  $-20^{\circ}$ . B.P. (1898) and U.S. limits are unjust, preventing many genuine oils from being sold.—Am. Jl. Ph., Feb., '08, 51. *Vide* also C.D. i./10, 293.

O.R. never below  $-16^{\circ}$  in 1500 samples.—Parry, C.D. ii. 11, 451.

*Off.* adopts  $-13^{\circ}$  to  $-21^{\circ}$ .

Sandal Wood Oils.—Am. Jl. Ph., 1911, p. 335.

### Copaiba.

*Off.* has Sp. Gr. 0.975 to 0.995.

For Maranham and Maracaibo varieties the Acid Number is at least 75. Para and Bahia varieties contain a greater proportion of volatile oil, consequently lower acid number.—Umney, C.D. ii./09, 579.

P.G.V. gives Acid No. 75.8 to 84.2, Saponification No. 84.2 to 92.7. Special directions for procedure in both cases are supplied.

**Test for Gurjun Balsam (*q.v.*).**—Dissolve four drops of the sample in 3 Cc. of glacial Acetic Acid, one drop of freshly made 10% Aqueous Potassium Nitrite Solution is added and the mixture poured carefully on to the surface of 2 Cc. of Concentrated Sulphuric Acid. A dark colour always appears, but in the presence of Gurjun Balsam a violet is formed in the clear upper layer.—Am. Jl. Ph., Jan. '08, 11.

P.G.V. gives this test slightly modified also, the following for added Oils:—Warm 1 Gm. of the Balsam on a water bath for an hour; on cooling to room temperature a brittle resin must remain.—Castor Oil has been used as adulterant.—Too stringent.—W. H. M.

For further details of Copaiba see *Oleum Santali*, Vol. I.

### OPIUM.

The ash of opium should not exceed 4% to 8%, moisture about 12%.

Turkish, Persian, Egyptian, and Indian Opium of Commerce.—Am. Jl. Ph., April, '07, 156. Capsules estimated.—Y.B.P. 1907, 131.

Estimation of Narcotine and Codeine in Opium.—Y.B.P. 1903, 122.

Of the 20 or more alkaloids in Opium, six are of more importance than the others. These occur in Turkey Opium as follows, approximately:—Morphine 9, Narcotine 5, Papaverine 0.8, Thebaine 0.4, Codeine 0.3, Narceine 0.2.—P.J. i./12, 161. See also Allen, 4th Edn., Vol. VI., 417.

Assay Process using Anhydrous Acetone for washing.—P.J. i./13, 367.

#### Modified Dowzard Process for Assay of Opium Tincture.

Evaporate 100 Cc. to 25 Gm. on water bath. Mix intimately on cooling 3 Gm. Calcium Hydrate with a small pestle. Transfer to flask graduated at 102 Cc. Shake well seven or eight times in the half hour's digestion. Filter off and pipette 50 Cc. to an oval flask with 30 Cc. Ether, 5 Cc. Alcohol 90%, and 2 Gm. Ammonium Chloride. Shake 30 minutes, stand over night, remove Ether layer with a straight pipette through inter-leaved filter papers, shake residue with 15 Cc. Ether. Again pipette off and wash papers with 5 Cc. Ether ( $0.720$ ) twice, thoroughly evaporate Ether from the papers and then filter aqueous residue (Morphine finally), washing pipette, etc. with 100 Cc. Morphinated water. Dry filter papers by identical compression. Digest each with 20 Cc. N/10 Sulphuric Acid, pulp the papers thoroughly, dilute

with water and back-titrate with N/20 Sodium Hydrate using Methyl Orange.

—H. R. Jensen, P.J. ii./13,876.

The presence of **Milk Sugar**, *i.e.*, as diluent of Opium may interfere markedly in the U.S. assay process.—C. H. La Wall, Jl. Am. Ph.A., May/1912,411; P.J. ii./12,75.

Starch also interferes.—P.J. ii./13,647.

In powdered Opium the amount of Morphine compounds insoluble in water appears to increase with age of the sample. Amount of total Morphine is also reduced.—P.J. ii./12 781.

**Standardisation of all the Active Constituents of Opium** suggested, *i.e.*, Morphine, Narcotine, Codeine and Meconic Acid, not on Morphine content alone.

The estimation of Meconic acid is colorimetric by means of (1) precipitation with Goulard's Extract; (2) subsequent comparison of the color produced with Ferric Chloride—using a control of pure Meconic Acid. The paper should be consulted.

As a result of the examination of four samples of Opium the author found:—

Morphine . . . .	12.2%	14.1%	10.5%	12.4%
Narcotine.. . .	5.8%	4.8%	6.8%	7.6%
Codeine . . . .	1.1%	0.7%	1.5%	0.9%
Meconic Acid . . . .	5.4%	4.3%	4.5%	6.4%

—P. Van der Wielen, P.J. ii./13,114.

### Estimation of Morphine in Omnopon and other Opiates.

Liberate the alkaloids by Sodium Bicarbonate and extract those other than Morphine by Chloroform saturated with Morphine; the Morphine is then extracted by a mixture of equal volumes of Isobutyl Alcohol and Chloroform, the extract is shaken with a known amount of standard Hydrochloric Acid, the excess of which is found by titration. The results are about 1.5% too high.—E. Anneler (Arch. Pharm., 1912,250, 186–198). J.C.S.A. ii./12, 819.

Estimation in Acid Liquids, *e.g.*, Sydenham's Laudanum of the Codex.—P.J. ii./13,881.

### Morphina.

To the phenolic character (chemically) of Morphine is due the coloration produced by Ferric Salts, its reducing effect on iron and on iodates—distinction from Codeine, Dionin and Heroin in which the Phenolic OH. has been replaced.—Am. Jl. Ph. Feb. 08,73.

For details of efforts at Synthesis of derivatives of Morphine (the structure of which is not known with certainty) *vide*—May, p. 104, *et seq.*

Estimation in presence of Glycerin by precipitating Morphine-di-iodo hydriodide (not "Morphine hydriodide tri-iodide," as stated.—W. H. M.)—Am. Jl. Ph. 1906,465.

Isolation of morphine in toxicology.—P.J. ii./05,617.

Morphine.—Solubility in Carbon Tetrachloride is 0.0156 Gm. in 100 Gm. at 18 to 22° C.—Y.B.P., 1913,6.

Spectrum lines characteristic for Morphine are obtainable with 1/200 grain.—J. J. Dobbie. L. i./13,1399.

For further details on Estimation *vide* Allen, 4th Edn., Vol. VI., 417–433.

① **Gregory's Salt**. An impure Morphine Hydrochloride being a mixture or double salt of Morphine Hydrochloride and Codeine Hydrochloride occurring in the manufacture of Morphine.—Hager.

② **Cryptopine**, ③ **Gnoscopine**, **Meconin**, ④ **Papaverine**, and ⑤ **Xantholine**—are other constituents of opium, *vide* Edn. xiv., p. 459.

⑥ **Laudanosine**. (another body).—Yields on oxidation \* **Lodal** *vide* Vol. I. For synthetic notes on these alkaloids see P. May, p. 103, *et seq.*

⑦ **Hydroxycodine**. *Syn.* **Neopine**. A new amorphous alkaloid found by T. and H. Smith in small quantity in the last Opium Alkaloid Mother liquors. Readily soluble in water, Alcohol, Ether and Chloroform. Hydrobromide and Hydrochloride both crystallise well.—J.C. S.T. '11,34.

### Apomorphinæ Hydrochloridum.

E. Schmidt says, although originally described as anhydrous he finds 3.61 to 3.95% H<sub>2</sub>O which cannot be accorded with either 2(C<sub>17</sub>H<sub>17</sub>NO<sub>2</sub>.HCl).H<sub>2</sub>O or C<sub>17</sub>H<sub>17</sub>NO<sub>2</sub>.HCl.H<sub>2</sub>O.—P.J. ii./08,516; B.P., 1914, has adopted the former.

Dott thinks the formula should be C<sub>34</sub>H<sub>36</sub>N<sub>2</sub>O<sub>5</sub>2HCl.2H<sub>2</sub>O (2 mols. Morphine minus 1 mol. H<sub>2</sub>O assumed to yield apomorphine) but says further investiga-



tion necessary. He found 5.21% loss on water bath; theory requires for  $2\text{H}_2\text{O}$  on his formula 5.44% loss.—P.J. ii./o8,801.

V. Paolini finds 4.2%  $\text{H}_2\text{O}$  as indicated by the formula  $\text{C}_{17}\text{H}_{17}\text{O}_2\text{N}.\text{HCl}$ ,  $\frac{3}{4}\text{H}_2\text{O}$ . He finds the formula for the base to be  $\text{C}_{17}\text{H}_{17}\text{O}_2\text{N}$ .—P.J. ii./13,809

A further note on formation of Apomorphine and Water Content by D. B. Dott.—P.J. i./14,164.

It is a very hygroscopic salt. We found that on drying and then placing over Calcium Chloride it reverted to the content of water originally present, viz., 3.4%.

## PANCREATINUM.

### THE EFFECT OF

#### CERTAIN CHEMICALS AND DRUGS ON THE ACTION OF PANCREATIN.

We conducted recently as supplementary to the work on Pepsin a number of experiments to determine which chemicals and "drugs" in a selected list prevent the proteolytic action of Pancreatin under certain conditions.

The substances chosen are almost identical with those in the Pepsin experiments. In the Pancreatin series, however, we omitted the acids, as these are generally held to be incompatible. W. M. Bayliss ('Nature of Enzyme Action') says Trypsin is practically inert in acid or neutral solution. Chittenden and Cummins however state (O. Hammarsten) that when the acid is combined with protein bodies digestion may take place rapidly when the acid combination is not in too great excess.

One quarter average doses of the substances were mixed with 5 ounces of a 3.5% Casein Solution prepared by aid of 0.35% Sodium Bicarbonate. 2 Cc. of an active Pancreatin Solution were then added. We have, therefore, the equivalent of an average dose of the "drug" in 570 Cc. (1 pint) of liquid, this bearing some relation to the conditions *in vivo*.

Milk is usually employed in standardising Pancreatin. We found it unsatisfactory and prefer the Casein method which we have arranged. Some of the chemicals in our selection cause a precipitation of the casein though the peptonising action may still proceed.

The sign + in the list indicates *complete peptonisation*—i.e., no precipitate in the liquor on acidifying with Nitric Acid a sample removed after 1 hour at 40° C.—in other words *compatibility*.

The — sign indicates that all the casein had not been peptonised as evidenced by a pp. occurring with Nitric Acid. These experiments showing, therefore, simply + and — are not so conclusive as the Pepsin series (*q.v.*) in which quantitative data are provided. The dilution used in the Pancreatin series is 20 times as great as that of List A in the Pepsin series. The incompatibles in the case of Pancreatin are more comparable with List C in the Pepsin experiments. The occurrence of a — sign with a drug in the Pancreatin series, together with a large proportion of undissolved albumen in the Pepsin series is interesting, as showing evidently marked physiological incompatibility.

The results were as follows :—

Chemical or Drug.	After 1 hour at 40° C.	Chemical or Drug.	After 1 hour at 40° C.
Acetonum .. ..	1·5 Cc. +	Liq. Bismuthi .. ..	0·6 Cc. +
Aether .. ..	0·5 Cc. +	„ Hamamelidis .. ..	1·2 Cc. +
Aethyl Acetas .. ..	1 Cc. +	„ Hydrogenii Per- oxidi 10 vols. .. ..	2·0 Cc. +
Alcohol .. ..	4 Cc. —	„ Morphinae Hydro- chloridi .. ..	0·5 Cc. +
Alum .. ..	0·16 Gm. +	„ Sennae Concent... ..	0·6 Cc. +
Auri Chloridum .. ..	0·0005 Gm. +	Lithii Citras .. ..	0·13 Gm. +
Caffeinae Citras .. ..	0·1 Gm. +	Lycetol .. ..	0·32 Gm. +
Calcii Chloridum .. ..	0·16 Gm. —	Magnesii Sulphas .. ..	1·0 Gm. —
„ Glycerophosph. .. ..	0·1 Gm. +	„ .. „ .. ..	0·13 Gm. +
Chinosol .. ..	0·06 Gm. +	Manganesii „Hypo- phosphis .. ..	0·13 Gm. —
Chloral .. ..	0·16 Gm. +	Methylene Blue .. ..	0·06 Gm. +
Chlorodyne... ..	0·15 Cc. +	Methyl Alcohol .. ..	0·25 Cc. +
Chloroform... ..	0·12 Cc. +	Migralgin .. ..	0·2 Gm. +
Cocain Hydrochlor... ..	0·008 Gm. +	Naphthaline Hydro- chlor. .. ..	0·2 Gm. +
Codeina „ .. ..	0·016 Gm. +	Paraldehydum .. ..	0·5 Cc. +
Creosotum .. ..	0·04 Cc. +	Phenacetin .. ..	0·12 Gm. +
Cupri Sulphas .. ..	0·1 Gm. —	Phenazonum .. ..	0·15 Gm. +
Dec. Aloes Comp. .. ..	4·0 Cc. +	Piperazin .. ..	0·12 Gm. +
Elixir Aromaticum .. ..	1·0 Cc. +	Podophyllin .. ..	0·02 Gm. +
„ Bismuthi and		Potassa Sulphurata .. ..	0·12 Gm. +
„ Pepsina .. ..	1·0 Cc. +	Potassii Bicarbonas .. ..	0·3 Gm. +
„ Papain .. ..	1·0 Cc. +	„ Bromidum .. ..	0·3 Gm. +
Ext. Cascarae Liq... ..	0·6 Cc. +	„ Chloras. .. ..	0·15 Gm. +
„ Cinchonae Liq. .. ..	0·2 Cc. +	„ Chloridum .. ..	0·3 Gm. +
„ Cocae Liq. .. ..	0·6 Cc. +	„ Citras .. ..	0·5 Gm. +
„ Ergotæ Liq. .. ..	0·3 Cc. +	„ Iodidum .. ..	0·15 Gm. +
„ Hydrastis Liq. .. ..	0·15 Cc. +	„ Permanganas .. ..	0·03 Gm. +
„ Ipecac. Liq. .. ..	0·3 Cc. +	Pyramidon .. ..	0·1 Gm. +
„ Malti Liq. .. ..	2·0 Cc. +	Pyrogallol .. ..	0·015 Gm. +
„ Nuclei Vomicae Liq. .. ..	0·03 Cc. +	Quinine Hydrochlor. .. ..	0·1 Gm. —
„ Opii Liq. .. ..	0·3 Cc. +	„ Bi-hydrochlor. .. ..	0·1 Gm. —
„ Suprarenal Liq. .. ..	0·2 Cc. +	Saccharin .. ..	0·008 Gm. +
„ Taraxaci Liq. .. ..	1·0 Cc. +	Salol .. ..	0·15 Gm. +
Fel Bovinum Purif. .. ..	0·15 Gm. +	Santonin .. ..	0·05 Gm. +
Ferri et Ammonii Citras .. ..	0·12 Gm. +	Sodii Arsanilas .. ..	0·03 Gm. +
„ Perchloridum .. ..	0·1 Gm. —	„ Cacodylas .. ..	0·015 Gm. +
„ et Quininae Citras .. ..	0·12 Gm. +	„ Chloridum .. ..	0·3 Gm. +
„ Sulphas... ..	0·12 Gm. +	„ Coumaras .. ..	0·05 Gm. +
Formalin .. ..	0·015 Cc. +	„ Methyl Arsonas .. ..	0·03 Gm. +
Glycerin .. ..	1·2 Cc. +	„ Nitris... ..	0·05 Gm. +
Glycosal .. ..	0·3 Gm. +	„ Sulphis. .. ..	0·16 Gm. +
Guaiacol .. ..	0·05 Cc. +	„ Thiosulphas .. ..	0·5 Gm. +
„ Camphorate .. ..	0·12 Gm. +	Stypticin .. ..	0·01 Gm. +
„ Carbonate .. ..	0·1 Gm. +	Syrupus Ferri Iodidi .. ..	0·6 Cc. —
Guarana .. ..	0·5 Gm. +	„ „ Phosphatis .. ..	0·6 Cc. —
Heroin Hydrochlor. .. ..	0·001 Gm. +	Terebene .. ..	0·2 Cc. +
Hexamethylenetetra- mine .. ..	0·16 Gm. +	Terpene Hydrate .. ..	0·06 Gm. +
Hydrarg. Potass Iodi- dum .. ..	0·0006 Gm. +	Thymol .. ..	0·05 Gm. +
Hydrarg. Perchloridum .. ..	0·0006 Gm. +	Theobromin Sodio Salicyl. .. ..	0·16 Gm. +
Hyoscinae Hydrobro- midum .. ..	0·0002 Gm. +	Thiocol .. ..	0·16 Gm. +
Iodol .. ..	0·03 Gm. +	Thiosinamin .. ..	0·03 Gm. +
Jalapin .. ..	0·03 Gm. +	Zinci Bromidum .. ..	0·05 Gm. —
Liquor Ammonia Citratris Fort .. ..	1·0 Cc. +	„ Sulphas .. ..	0·03 Gm. —
„ Arsenici Hydro- chloric .. ..	0·12 Cc. +		



It will be evident that a better view of the relative incompatibility of Pancreatin with the substances in question is obtained by comparing the Pancreatin Incompatibles with the Pepsin results (Lists A and D together) thus :—

<i>Inhibit Action of Pancreatin in dilute condition.</i>			<i>Result with Pepsin in Dilute concentration—'List D,' and Strong Concentration—'List A.'</i>
Alum	0.16 Gm. in 150 Cc. (5 ozs.)		Compatible (List D)
Calcii Chloridum	0.16 Gm. „ „ „		Practically Compatible (List A).
Cupri Sulphas	0.1 Gm. „ „ „		Compatible (List D).
Ferri Perchlorid	0.1 Gm. „ „ „		„ „
Magnesii Sulphas	1.0 Gm. „ „ „		Inhibits to Extent of 35% undissolved (List D).
Manganes. Hypoph.	0.13 Gm. „ „ „		Practically Compatible (List A).
Quininæ HCl.	0.1 Gm. „ „ „		Practically Compatible (List A).
Syr. Ferri Iodidi.	0.6 Cc. „ „ „		Compatible (List A).
„ „ Phosph.	0.6 Cc. „ „ „		„ „
Zinci Bromidum	0.05 Gm. „ „ „		„ (List D).
„ Sulphas	0.03 Gm. „ „ „		„ „

#### *Conclusions.*

It will be seen that these results are very similar—the total list of incompatibles is very much on the same lines in both series. The majority of the Pancreatin Incompatibles appear in the Pepsin Lists as incompatible also, though not to so marked a degree—Alum, Copper Sulphate, Ferric Chloride, Zinc Bromide, and Sulphate were more incompatible with Pancreatin than with Pepsin. Similarly, Syrup of Ferrous Iodide and Syrup of Ferrous Phosphate were incompatible with Pancreatin, whilst they were compatible with Pepsin.

Magnesium Sulphate figures as incompatible with both ferments in the same dilutions. 'Acids' in general may here be added:

*C.f.* also Pepsin Results, p. 115 *et seq.* and 'Enzyme Action,' Vol. I., p. 601.

#### EXPERIMENTS TO DETERMINE EFFECT OF CHEMICALS ON THE AMYLOLYTIC ACTION OF PANCREATIN.

It seemed of interest to determine the amylolytic activity of a *Pancreatin which had been found to be weak in proteolytic power* and then subsequently to determine the inhibitory effect of drugs on the amyololysis.

With regard to the first point it was found that the sample of Pancreatin in question was well up to Standard when tested for amylolytic power; and a certain liquid preparation of commerce, which had strong proteolytic power, was found to be practically useless for amyololysis. *C.f.* Malt Diastase Results.

As to the second point, 0.4 Gm. of the Pancreatin, weak in proteolytic power, was mixed with 10 Cc. of Water, and added to Starch 7.5 Gm. gelatinised in water 150 Cc. (made almost transparent by boiling and cooling)—the amount of medicament having been previously added to this Starch mixture.

After 5, 15 and 30 minutes the liquors were tested with dilute Iodine Solution on the lines of the U.S. P. Test. Results were as follows :—

		5 minutes.	15 minutes.	30 minutes
Acid	Aceto-Salicylicum 0.16 Gm.	—	—	—
"	Gallicum 0.16 Gm.	—	—	—
"	Hydriodicum Dil. 0.15 Cc.	—	partial.	partial.
"	Hydrobromicum 0.5 Cc.	—	—	—
"	Hydrochlor. Dil. 0.15 Cc.	—	—	—
"	Salicylicum 0.16 Gm.	+	—	—
"	Tannicum 0.16 Gm.	—	—	—
Alum (Potash)	0.16 Gm.	partial.	partial.	+
Caffeinæ Citras	0.08 Gm.	partial.	partial.	+
Cupri Sulphas	0.1 Gm.	—	—	partial.
Ferri Perchloridum	0.1 Gm.	—	—	—
Piperazine	0.16 Gm.	—	partial.	partial.
Potassa Sulphurata	1.3 Gm.	+	—	—
Potassii Bicarbonas	1.3 Gm.	+	—	—
Syr. Ferri Iodidi	0.6 Cc.	+	—	—
" " Phosph.	0.6 Cc.	+	—	—
Zinci Bromidum	0.05 Gm.	+	—	—
" Sulphas	0.03 Gm.	+	—	—

Pancreatins of commerce vary greatly—many are almost inert. Sorensen's Test recommended. 0.02 Gm. after 1 hour's digestion should require 2 Cc. of N/5 NaOH under conditions of the test. See Pract. Phys. Chem.—Aders Plimmer, also B.M.J. i./12,584.

The Milk Test in the U.S.P. test for Pancreatin is unreliable.—Am. Jl. Ph. Nov. 11,524.

Measurement of relative tryptic activity by Sorensen's Method. Five specimens of Pancreatin and two of Trypsin compared.—A. R. Smith, P.J. ii./12,137.

Some commercial varieties of Pancreatin yield to peptonised milk an objectionable odour.—T. E. Tawell points out that this is due to the fact that the cheap forms of Petroleum are used in extracting fat from Pancreatin.—B.J. ii./13,570.

#### Muller's Trypsin Test.

A method of testing the activity of Trypsin Preparations consists in placing small quantities of the Trypsin preparations to be tested from a Platinum loop, upon a Löffler Blood Serum plate and incubating 12 hours at 55 to 60° C. In good products a depression should be made on the Serum with a dilution 1:1000.—Pr. Jan., 1913.—Tuberculos No.

### PARAFFINUM LIQUIDUM.

Off. now allows a larger range of Sp. Gr., viz., 0.860 to 0.890 (B.P. '98 was 0.885 to 0.890).

Liquid Paraffin has latterly been largely used as an intestinal lubricant. A light oil is not advised for this purpose. We deal fully with the matter in Vol. I.

Liquid Paraffin may be used in place of Cedar Wood Oil for lens immersion.—Rowntree.

There is no better mounting medium for bacteria. The refractive index of bacteria is said to be 1.55, Canada Balsam 1.538, Balsam in Xylol a little lower say 1.53, Distilled Water 1.336, Liquid Paraffin 1.471. In a medium exactly that of the bacteria, e.g., Oil of Aniseed 1.55 the bacteria (dried) but unstained



would be invisible, in Canada Balsam they would be seen, in Paraffin better and in Water best. Flagella of bacteria and spirochaetae which were known to possess same, as well as the flagella of the tubercle bacillus and *M. Meitensis* (which are commonly supposed not to possess them) were taken in some test experiments. The visibility of same (the bacteria being stained by ordinary stains, not flagella stains) depended largely on the mounting medium used. These were not easily seen in media of *very high or very low R.I.*, but these media caused very rapid fading. Of all practical media Parolein was found to be best. Liquid Paraffin is, however, not so good as Cedar Wood Oil for lens immersions.—A.C.Coles —L.i./II,877.

‘**Petrol**’ and **Petrol Tests**.—Fractionation shows sophistication. A uniform B. Pt. and Sp. Gr. to the last residue is the ideal. A good petrol has Sp. Gr. 0.680 to the last 10%, which is 0.715. The B.Pt. of this is about 75° C.—all being over at 85° C. (the last 10%). ‘**Motor Spirit**’ may have given fractions with larger ranges of Sp. Gr. and B. Pts.—Bailie, Automotor Jl., May 23,08.

## PEPSINUM.

*Off.* Pepsin has the same standard as B.P. '98, viz., 1 digests 2,500 of hard boiled egg albumen, but the process is now different.

### Further Assay Methods:—

FR. CX. requires that the Pepsin shall convert 25 times its weight of dried fibrin. Pepsin 0.1, Dilute Hydrochloric Acid 1.5, Water 58.5, Fibrin 2.5 for 9 hours at 50°. Test filtrate with Nitric Acid. Pepsin Amylacée and Pepsin Lactosée in dose 0.25 Gm. are to contain sufficient Pepsin to carry out the above test.

Hercod and Maben, comparing the official methods in various countries, suggest as an International standard 1 to 2,000 and *Assay Method* as follows:

Coagulated white of egg (obtained by boiling fresh eggs for ten minutes), pass through a No. 40 sieve, and press between two sheets of filter-paper to remove surplus moisture; place 10 Gm. in a 200 Cc. flask containing 100 Cc. of distilled water previously heated to 52° C., 0.25 per cent. absolute HCl, and 5 Cc. of a 0.1 per cent. solution of pepsin. Place the flask in a water-bath at 52° C., and digest at that temperature for two hours, stirring gently every fifteen minutes with a rotatory movement by means of a glass rod. At the expiration of two hours the albumin should be dissolved, the solution having an opalescent appearance.—P.J. ii./10,368; C.D. ii./10,371.

It is stated (Maben and Walker C.D. Sept. 3 1910, p. 41), that on digesting albumin with Pepsin (in acid solution) the albumin is not entirely converted into Peptone—on the contrary, firstly, Syntonin and secondly Proteose (Albumose) are formed prior to Peptone: even if the digestion is carried on for as long as 144 hours rarely “more than 45% of true peptone is in solution.”

The Syntonin can be demonstrated by neutralising the acid solution with alkali—whitish precipitate

The albumose can be shown by treating with hot saturated solution of Ammonium Sulphate.

Carmino-fibrin, prepared by washing blood fibrin with ammoniacal solution of carmine, is a dark coloured mass, easily crumbled, which yields no colour to water or 0.1% Hydrochloric Acid until the fibrin contained in it has been dissolved by a ferment; hence its use as a simple quantitative test for pepsin by noting the time required to give a pink colour equal to that of a standard or control.

### THE EFFECT OF CERTAIN CHEMICALS AND DRUGS ON THE ACTION OF PEPSIN.

The following experiments which we have recently conducted show approximately the relative inhibitory action *in vitro* which certain chemicals and drugs have on the digestive power of Pepsin. The conditions under which the experiments were conducted were as follows:—

Three Gm. of Egg Albumen, prepared as for testing Pepsin (*Off.*), were placed in 30 Cc. of Hydrochloric Acid 0·2%. An average dose (in most cases) of the drug was added, followed by 1 Cc. of freshly prepared Pepsin Solution containing 0·2% of Pepsin (*Off.*). These mixtures were then incubated at 38° C. for fifteen hours, this length of time being allowed to permit of the Pepsin utilising its power to the utmost. It is to be noted that 30 Cc. of fluid is a minute amount in comparison with the capacity of the human stomach, but the results are comparable, and it is evident that if the drugs in question do not interfere with peptic activity in this strong concentration, they are certainly not likely to do so when more diluted. On the other hand, if peptic activity is interfered with, there is evidence of physiological incompatibility—though it may be of less magnitude than the figures suggest.

## List A.

Chemical or Drug.	Undissolved Albumen after 15 hours.	Percentage Undissolved.
	Gm.	
Acetone 6·0 Cc. . . . .	1·5	50·00
„ 3 Cc. . . . .	0·10	3·33
„ 2 Cc. . . . .	Trace.	Negligible.
Acid „ Aceto Salicyl 0·6 Gm. . . . .	0·05	1·66
„ Aceto-Coumaric 0·6 Gm. . . . .	0·34	11·33
„ Benzoic 0·6 Gm. . . . .	0·03	1·00
„ Boric 0·6 Gm. . . . .	0·00	0·00
„ Cacodylic 0·12 Gm. . . . .	0·20	6·66
„ Carbolic 0·2 Gm. . . . .	0·20	6·66
„ Citric 0·3 Gm. . . . .	0·40	13·33
„ Coumaric 0·6 Gm. . . . .	0·30	10·00
„ Gallic 0·6 Gm. . . . .	0·15	5·00
„ Hydriodic Dil. 0·6 Cc. . . . .	0·40	13·33
„ Hydrochloric Dil. 0·35 Cc. (10%) . . . . .	0·10	3·33
„ Hydrobromic 2 Cc. (10%) . . . . .	0·35	11·66
„ Hypophosph. Dil. 0·5 Cc. . . . .	0·10	3·33
„ Phosph. Conc. 0·25 Cc. (66%) . . . . .	0·10	3·33
„ Salicylic 0·3 Gm. . . . .	0·15	5·00
„ Sulphurosum 2 Cc. (5%SO <sub>2</sub> ) . . . . .	0·15	5·00
Æther 2 Cc. . . . .	0·05	1·66
Æthyl Acetas 4 Cc. . . . .	0·50	16·60
Alcohol 90% 15·0 Cc. . . . .	2·65	88·33
„ 90% 8 Cc. . . . .	1·00	33·33
„ 90% 4 Cc. . . . .	0·40	13·33
„ 90% 0·6 Cc. . . . .	0·24	8·00
Alum 0·6 Gm. (Potash) . . . . .	2·00	66·66
Auri Chloridum 0·002 Gm. . . . .	0·00	0·00
Bismuth, see Liquor Bismuthi.		
Caffeinæ Citras 0·3 Gm. . . . .	0·04	1·33
Calcii Chloridum 0·6 Gm. . . . .	0·30	10·00
„ Glycerophosph. 0·3 Gm. . . . .	0·00	0·00
Chinosol 0·2 Gm. . . . .	0·95	31·66
Chloral Hydras 0·6 Gm. . . . .	0·30	10·00
Chloromorphiæ Liquor 0·6 Cc. . . . .	0·10	3·33
Chloroform 0·5 Cc. . . . .	0·10	3·33
Cocainæ Hydrochloridum 0·03 Gm. . . . .	0·00	0·00
Codeinæ Hydrochloridum 0·06 Gm. . . . .	Trace.	Negligible.
Creosotum 0·2 Cc. . . . .	0·25	8·33
Cupri Sulphas 0·3 Gm. . . . .	1·20	40·00



## List A—continued.

Chemical or Drug.	Undissolved Albumen after 15 hours.	Percentage Undissolved.
Decoctum Aloes Comp. 15·0 Cc. . . . .	Gm. 1·00	33·00
Elixir Aromaticum 4 Cc. . . . .	Trace.	Negligible.
„ Papain 4 Cc. . . . .	0·14	4·66
Ext. Cascaræ Liquidum 3 Cc. . . . .	0·20	6·66
„ Cinchonæ Liquidum 0·7 Cc. . . . .	Trace.	Negligible.
„ Cocæ Liquidum 3 Cc. . . . .	„	„
„ Ergotæ Liquidum 1·5 Cc. . . . .	„	„
„ Hydrastis Liquidum 0·6 Cc. . . . .	„	„
„ Ipecac. Liquidum 1·0 Cc. . . . .	„	„
„ Malti Liquidum 8 Cc. . . . .	3·00	100·00
„ Nucis Vom. Liq. 0·12 Cc. . . . .	Trace.	Negligible.
„ Opii Liq. 1·2 Cc. . . . .	0·24	8·00
„ Suprarenal Liq. 0·7 Cc. . . . .	0·49	16·33
„ Tarax. Liq. 4 Cc. . . . .	1·61	53·66
Fel Bovinum 0·6 Gm. . . . .	3·00	100·00
Ferri et Ammon. Cit. 0·5 Gm. . . . .	2·73	91·00
„ et Quinina Cit. 0·5 Gm. . . . .	3·00	100·00
„ Perchloridum 0·4 Gm. . . . .	2·40	80·00
„ Sulphas. 0·2 Gm. . . . .	1·66	55·33
Formalin 0·06 Cc. . . . .	0·43	14·33
Glycerin 5·0 Cc. . . . .	0·28	9·33
Glycerin. Trypsin 5·0 Cc. . . . .	0·40	13·33
Glycetract Calumbæ 1·0 Cc. . . . .	0·10	3·33
Glycosal 1·2 Gm. . . . .	1·12	37·33
Guaiacol 0·20 Cc. . . . .	1·51	50·33
Guaiacol Camphoras 0·5 Gm. . . . .	Trace.	Negligible.
Guaiacol Carbolas. 0·3 Gm. . . . .	„	„
Guarana 2·0 Gm. . . . .	„	„
Helmitol 0·5 Gm. . . . .	1·76	58·66
Heroin Hydrochlor. 0·003 Gm. . . . .	0·00	0·00
Hexamethylene tetramine 0·6 Gm. . . . .	1·50	50·00
Hydrargyri Potass. Iodid. 0·0025 Gm. . . . .	0·00	0·00
„ Perchloridum 0·0025 Gm. . . . .	0·00	0·00
Hyoscinæ HBr. 0·0006 Gm. . . . .	0·00	0·00
Iodol 0·12 Gm. . . . .	Trace	Negligible.
Jalapin 0·12 Gm. . . . .	1·30	43·33
L quor Ammonii Citras Fort. 4 Cc. . . . .	2·30	76·66
Hydrogenii Peroxidi Liquor (' 10vol.')		
8·0 Cc. . . . .	0·00	0·00
Liq. Arsenii Hydrochloricus 0·5 Cc. . . . .	0·05	1·66
„ Bismuthi 3 Cc. . . . .	0·50	16·66
„ Hamamelidis 5 Cc. . . . .	0·00	0·00
„ Morphinæ Hydrochlor 2 Cc. . . . .	Trace.	Negligible.
„ Sennæ Conc. 3 Cc. . . . .	2·40	80·00
Lithii Citras 0·5 Cc. . . . .	1·80	60·00
Lycetol 1·2 Gm. . . . .	2·10	70·00
Magnesii Sulphas 4·0 Gm. . . . .	1·90	63·33
„ „ 0·6 Gm. . . . .	1·15	38·33
Manganesii Hypophosph. 0·5 Gm. . . . .	0·40	13·33
Methylene Blue 0·25 Gm. . . . .	0·19	6·33
Methyl Alcohol 1·0 Cc. . . . .	Trace.	Negligible.
Migralgin 0·8 Gm. . . . .	0·20	6·66
Naphthalini Hydrochlor. 0·6 Gm. . . . .	0·00	0·00
Pancreatin 0·25 Gm. . . . .	0·00	0·00
Paraldehydum 2 Cc. . . . .	1·60	53·33
Perhydrol 2 Cc. . . . .	0·00	0·00
Phenacetinum 0·5 Gm. . . . .	0·00	0·00
Phenazonum 0·6 Gm. . . . .	1·40	46·66

## List A—continued.

Chemical or Drug.	Undissolved Albumen after 15 hours.	Percentage Undissolved.
Phosphorus 0·0013 Gm. . . . .	Gm. 0·00	0·00
Physostigminæ Sulph. 0·002 Gm. . . . .	0·00	0·00
Picrotoxin 0·001 Gm. . . . .	0·00	0·00
Pilocarpinæ Nitras 0·003 Gm. . . . .	0·00	0·00
Piperazina (Base) 0·5 Gm. . . . .	2·45	81·66
„ (neutralised with HCl) 0·5 Gm. . . . .	0·73	24·33
Podophyllin 0·06 Gm. . . . .	0·00	0·00
Potassa Sulphurata 0·4 Gm. . . . .	2·60	86·66
„ „ (Neutralised with HCl) . . . . .	1·90	63·33
Potassii Bicarbonas 1·2 Gm. . . . .	1·70	56·66
„ Bromidum 1·2 Gm. . . . .	1·64	54·66
„ Chloras 0·6 Gm. . . . .	1·14	38·00
„ Chloridum 0·3 Gm. . . . .	1·20	40·00
„ „ 0·6 Gm. . . . .	2·10	70·00
„ „ 1·2 Gm. . . . .	2·40	80·00
„ Citras 2·0 Gm. . . . .	1·66	55·33
„ Iodidum 0·6 Gm. . . . .	1·90	63·33
„ Permanganas 0·12 Gm. . . . .	1·70	56·66
Pyramidon 0·3 Gm. . . . .	Trace.	Negligible.
Pyrogallol. 0·06 Gm. . . . .	„	„
Quininæ Hydrochlor. 0·3 Gm. . . . .	0·30	10·00
Saccharin 0·03 Gm. . . . .	0·42	14·00
Salol 0·6 Gm. . . . .	0·60	20·00
Santonin 0·2 Gm. . . . .	0·40	13·33
Sodii Arsauilas 0·12 Gm. . . . .	0·20	6·66
„ Cacodylas 0·06 Gm. . . . .	0·13	4·33
„ Chloridum 0·3 Gm. . . . .	0·80	26·66
„ „ 0·6 Gm. . . . .	1·50	50·00
„ „ 1·2 Gm. . . . .	1·70	56·66
„ Coumaras 0·2 Gm. . . . .	2·90	96·66
„ Methyl-Arsonas 0·12 Gm. . . . .	0·40	13·33
„ Nitris 0·1 Gm. . . . .	2·40	80·00
„ Sulphis 0·6 Gm. . . . .	2·50	83·33
„ Thiosulphas 2·0 Gm. . . . .	1·20	40·00
Stypticin 0·06 Gm. . . . .	Trace.	Negligible.
Syrupus Ferri Iodidi 2 Cc. . . . .	0·00	0·00
Terebenum 0·6 Cc. . . . .	0·10	3·33
Terpini Hydras 0·25 Gm. . . . .	0·30	10·00
Terpinol 0·2 Cc. . . . .	0·10	3·33
Theobromina 0·2 Gm. . . . .	Trace.	Negligible.
Theobrominæ Sodii Salicyl. 0·8 Gm. . . . .	2·05	61·66
Thiocol. 0·6 Gm. . . . .	2·45	81·66
Thiosinamin 0·1 Gm. . . . .	Trace.	Negligible.
Thymol 0·1 Gm. . . . .	1·80	60·00
Zinci Bromidum 0·2 Gm. . . . .	1·45	48·33
„ Sulphas. 0·12 Gm. . . . .	1·46	48·66
Control . . . . .	Nil.	Nil.

These results are interesting, as they tend to solve a vexed problem—to wit, the physiological incompatibility of a number of substances with Pepsin.



It is notable, for example, that the following apparently *do not interfere* with peptic activity to any extent :—

## List B.

Acetonum, small dose.	Guarana.
Acidum Aceto-Salicylicum.	Heroin Hydrochloridum.
„ Benzoicum.	Hydrargyri Perchloridum.
„ Boricum.	„ et Potassii Iodidum.
„ Cacodylicum.	Hydrogenii Peroxidum.
„ Carbohicum.	Hyoscinae Hydrobromidum.
„ Gallicum.	Iodol.
„ Hydrochloricum.	Liquor Arsenici Hydrochloricus.
„ Hypophosphorosum Dilutum.	„ Hamamelidis.
„ Phosphoricum.	„ Morphinae Hydrochloridi.
„ Salicylicum.	Magnesii Sulphas. ( <i>small dose.</i> )
„ Sulphurosum.	Methyl Alcohol.
Æther.	Methylene Blue.
Alcohol, small proportion.	Migralgin.
Auri Chloridum.	Naphthalini Hydrochloridum.
Caffeinae Citras.	Pancreatinum.
Calcii Glycerophosphas.	Perhydrol.
Chloromorphiæ Liquor.	Phenacetinum.
Chloroformum.	Phosphorus.
Cocainæ Hydrochloridum	Physostigminæ Sulphas.
Codeinæ Hydrochloridum.	Picrotoxinum.
Elixir Aromaticum.	Pilocarpinae Nitras.
„ Papain.	Podophyllin.
Extractum Cascara Liquidum.	Pyramidon.
„ Cinchonæ Liquidum.	Pyrogallol.
„ Cocæ Liquidum.	Sodii Arsanilas.
„ Ergotæ Liquidum.	„ Cacodylas.
„ Hydrastis Liquidum.	Stypticin.
„ Ipecacuanhæ Liquidum.	Syrupus Ferri Iodid.
„ Nucis Vomicae Liquidum.	Terebenum.
Glycetractum Calumbæ.	Terpinol.
Guaiacol Camphoras.	Theobromina
„ Carbonas.	Thiosinamin.

In arriving at the above conclusion we took, in most cases, 6·6 %, or less *undissolved* to indicate in the conditions of the test *physiological compatibility*. The gradation of figures in respect of the different amounts of Alcohol (see Table) is particularly interesting and instructive. The fact that Acids in general other than Hydrochloric are seen to be compatible is of interest. The compatibility of Chloroform is well known to physiological chemists. Other interesting and perhaps unexpected *compatibles* are Creosote Ether, Guaiacol preparations, Mercuric Chloride (in dose specified), Hydrogen Peroxide, Sodium Arsanilate.

The following, on the other hand, *inter alia*, appear to *prevent peptic action* if present in strong proportion :—

## LIST C.

Acetonum, large proportion.	Ferri Sulphas.
Alcohol, large proportion.	Guaiacol.
Alkalis.	Hexamethylentetramin.
Alumen.	Jalapin.
Cupri Sulphas.	Liquor Ammonii Citratis Fortis.
Extractum Malti.	„ Sennæ Concentratus
Fel Bovinum.	Lithii Citras.
Ferri et Ammonii Citras.	Magnesi Sulphas, in large dose.
„ et Quininæ Citras.	Paraldehydum.
„ Perchloridum.	Phenazonum.

Piperazina (Base).  
 Potassa Sulphurata (neutralised with  
 Hydrochloric Acid.)  
 Potassii Bromidum.  
 „ Chloras.  
 „ Chloridum  
 „ Citras.

Potassi Iodidum.  
 „ Permanganas.  
 Sodii Chloridum,—a considerable  
 amount.  
 „ Nitris.  
 „ Sulphis.  
 „ Thiosulphas

Amongst this series of particular interest are the results with **Alcohol, Sodium and Potassium Chlorides** (the Potassium Salt no better than the Sodium analogue), also **Hexamethylenetetramine** and **Magnesium Sulphate**. But one must take into account the comparatively strong concentrations in which we were working (an average dose of the drug in 30 Cc. of Peptonising Fluid) and the fact that such concentrations would hardly occur in practice. Nevertheless, as already stated, the evidence of these physiological incompatibilities is of value especially when the results are compared with the previous series, *i.e.*, the *relatively compatible* medicines.

We next tested whether the drugs that are incompatible in strong proportion (average dose in 30 Cc.) would exhibit similar effect when present in a volume of Liquid bearing more resemblance with that encountered in the human digestive tract.

For this purpose the drugs required from "List C" with some additions from "List A" were treated as follows:—

14·2 Gm. Egg Albumen prepared as before were placed in 150 Cc. of Hydrochloric Acid 0·2% containing 10 mgr. of Pepsin and  $\frac{1}{4}$  of an average dose (in most cases) of the drug was added. In other words, the conditions of the test are identical with those at the outset except that we have here the equivalent of the average dose of the drug approximately in a pint of the Liquor, whilst previously it was present in about an ounce (30 Cc.).

The results were as follows:—

#### LIST D.

Chemical or Drug.	Undissolved Albumen after 15 hours.	Percentage Undissolved.
Alum, 0·15 Gm. . . . .	Nil.	Nil.
Cupri Sulphas 0·1 Gm. . . . .	Nil.	Nil.
Ext. Malti Liq. 2 Cc. . . . .	Nil.	Nil.
Fel Bovinum Purif. 0·15 Gm. . . . .	0·4 Gm.	2·8%
Ferri et Ammon. Citras 0·13 Gm. . . . .	Nil.	Nil.
„ et Quinin. Citras 0·13 Gm. . . . .	Nil.	Nil.
„ Perchloridum 1·0 Gm. . . . .	Nil.	Nil.
„ Sulphas. 0·05 Gm. . . . .	Nil.	Nil.
Helmitol 0·15 Gm. . . . .	Nil.	Nil.
Hexamethylenetetramine 0·15 Gm. . . . .	1·7 Gm.	11·9%
Liq. Ammon. Citrat. Fort. 1 Cc. . . . .	11·5 Gm.	81%
Magnesii Sulphas 1 Gm. . . . .	5 Gm.	35%
Paraldehydum 0·5 Cc. . . . .	Nil.	Nil.
Phenazonum 0·15 Gm. . . . .	Nil.	Nil.
Piperazina (base) 0·15 Gm. . . . .	Nil.	Nil.
Potassa Sulphurata 0·1 Gm. . . . .	0·5 Gm.	3·5%
Sodii Nitris 0·02 Gm. . . . .	Trace.	Negligible.
„ Sulphis 0·15 Gm. . . . .	Nil.	Nil.
„ Coumaras 0·05 Gm. . . . .	Nil.	Nil.
Thiocol 0·15 Gm. . . . .	Nil.	Nil.
Zinci Bromidum 0·05 Gm. . . . .	Nil.	Nil.
„ Sulphas 0·02 Gm. . . . .	Nil.	Nil.
Control . . . . .	Nil.	Nil.



### Conclusions.

*Dilution* of the chemical or drug, therefore, plays a very important part in the matter. All the incompatible substances indicated in 'List C' were under exceptional circumstances of concentration.

'List D' shows that in the presence of a larger volume of diluent fluid the substances incompatible with Pepsin are greatly reduced in numbers, but the result in the case of **Magnesium Sulphate** is of peculiar interest. The proportions of undissolved albumen shown by the other substances in this list are negligible, or may be chemically explained.

It must not be forgotten that nature might compensate effects produced by chemicals in a manner which it is impossible to imitate in such experiments.

At the same time it must not be overlooked that under certain conditions, *e.g.* ill health, or an empty stomach, the volume of diluent fluid might be greatly reduced, hence the 'List A,' and in particular 'List C,' will be of value to the physician, *firstly*, as showing where incompatibility with the patient's peptic activity may be expected, and *secondly* when prescribing pepsin preparations, as showing what to avoid. These results may be compared with the analogous Pancreatin data.—*v.* also Malt, p. 79 *et seq.*

See also 'Enzyme Action' Vol. I. p. 601.

REFERENCES.—Enzymes, Proteins, Milk and Meat products.—Allen, 4th Edn., 1914, Vol. VIII.; also W. M. Bayliss & O. Hammarsten.

## PINUS.

### Oleum Terebinthinæ.

**Lævo-Pinine** or **Terebentene** of Berthelot is obtained by Fractionation of French Oil of Turpentine as a colourless mobile liquid of characteristic odor. Sp. Gr. 0.8767 at 0° C. and 0.8619 at 17.9° C.

**Dextro-Pinene** or **Australene**, the principal constituent of American Turpentine has the same Sp. Gr. and boiling point, etc., as the French. O.R. is stated to be + 2.15°.—Allen, Vol. II., Part II., I., p. 262.

**Russian Turpentine Oil.**—Authentic samples contain 40 to 70% distilling between 155° and 160° C. and consisting chiefly of Pinene. The oils arriving in the London markets have these 'middle runnings' removed.

For MAKING DISINFECTANTS it may not be of importance to have a large amount of hydrocarbon of relatively low boiling point. Useful details tabulated.—E. J. Parry, C.D. ii./12,340,655; Y.B.P. 1913,93; see also Vol. I., p.616.

## PIX LIQUIDA.

### Oleum Cadinum.

The following *Characters and Tests* are suggested:—

A vegetable tar obtained by dry distillation of *J. Oxycedrus*, of brownish red colour, transparent, clear and homogeneous aspect, has a wood-smoke-like odour, with a density inferior to water. It is almost *insoluble* in Water, but gives it an acid reaction, partly soluble in cold Alcohol, completely soluble in hot Alcohol (90%), in Ether, Chloroform and Carbon Bisulphide. The acidity expressed as Acetic Acid must not exceed 1.5 per 100Cc. It must be free of other Tars and particularly not give the **Copper Acetate Test** for foreign **Wood Tars and Resins**.—Shake out with Petroleum Ether, filter and shake filtrate with equal volume of 1% solution of Copper Acetate; the Petroleum layer is coloured green if wood tar be present.—Perfumery and Essential Oil Record, April, 1911.—P.J. i./11,567. A test on these lines is now adopted, *Off.*

We found on testing an assumed genuine sample, which gave no indication by itself, that *at least* 20% of Wood Tar (Stockholm) had to be added to give a definite green color to the dark supernatant liquor. There was no appreciable difference between the sample and the same adulterated with 10% of Stockholm Tar. Oleum Betulæ Pyroligneum gave a deep olive green color. Creosote, Phenol and Oleum Picis Rectificatum were tested and found to give no colour at all.

**Uses.**—Recommended in eczema and other skin affections, also for gout and rheumatism.

## PLUMBUM.

### Lead Poisoning.

Lead poisoning amongst yarn workers.—B.M.J. i./06,310.

Lead poisoning and the race.—Amongst a host of facts and fancies put forward, the following appears. Where (in Hungary) death from convulsions in early infancy rarely occurs, epilepsy is found later on to be more frequent in the children of potters than in those of non-potters.—B.M.J. i./11,1096.

Lead poisoning in all forms well treated by Calcium Permanganate in doses of  $\frac{1}{4}$  grain.—B.M.J., May 14./10,1166.

English Potteries, Lead Poisoning in, Home Office Report on.—B.M.J. ii./11,44. See also Na. Dec. 29, 1910, p. 273—a review on dangers attendant on the use of Lead and injury to health from dust and other causes in the manufacture of earthenware and china, etc. “It cannot be said that any real progress has been made. Although a large amount of earthenware can be made without the use of any lead, and even in the cases where lead must be used, it has been proved that the lead may be so combined that it is practically innocuous, the manufacturers as a body have hitherto resisted any attempt to prescribe a schedule of articles which should be made with leadless glaze, or to bind themselves to use glazes in which the lead is in an innocuous form. They demand unrestricted liberty to use any materials they think necessary for their purposes. The loud cry of “foreign competition” is sufficient to drown the still small voice of pity on behalf of the workers.. Lead glaze is the main source of the evil. The net upshot of the inquiry is that the whole position is not one whit ameliorated; the operatives apparently are still to remain the victims of lax surveillance or of indifference, and of official non-interference. If the manufacturers’ claim for unrestricted liberty is to be allowed they must be made to feel the responsibility they thereby incur by far more stringent measures than have hitherto been brought to bear upon them.” Anti-dust measures essential.—In industries using lead where much dust occurs lead poisoning is frequent,—the main avenue of entrance of the poison being the lungs.—T. M. Legge and K. W. Goadby.—B.M.J. ii./12,1712; L. i./13,183.

## PODOPHYLLI INDICI RHIZOMA *Off.* See also Vol. I. p. 629.

(*Podophyllum Emodi*.)

Physiologically *P. Emodi* is quite as active as the American *P. peltatum*. Picropodophyllin to the extent of 5.43% was obtained from Indian root collected after flowering, corresponding to an equal weight of Podophyllotoxin (with which it is isomeric). The resin yield was 10.79%—indicating a proportion of 50.3% of Picropodophyllin, whilst that in *P. peltatum* averages only about 20—25%. Picropodophyllin is not an actual constituent of the drug, but is formed by decomposition of Podophyllotoxin, which, together with Podophyllo-resin, an indefinite amorphous substance, represents the activity of the drug. ‘Fall-dug’ *P. peltatum* is preferred in America.—Umney, P.J. ii./11,156; C.D. ii./09,385.

T. A. Henry says action of both is due to Podophyllotoxin (purgative) and Podophyllo-resin (purgative and cholagogue). The Indian is richer in the former. Estimation process for Podophyllotoxin.—J.C.S., 1898,73, p.209. Previous references on this subject.—Y.B.P., 1892, p. 398. C.D. ii./09,487,522.

*P. Emodi* roots from the N.W. province of India gave 11.07 and 11.17% total resin. The proportion of Podophyllotoxin was in the first case 4.7% in the other 3.1%.—P.J. ii./12,579.



**POTASSIUM.****Alcoholic Solution of Potassium Hydroxide Solution for analytical work.**

Dissolve required amount of Potassium Hydroxide in its own weight of water and pour the solution when cold into Alcohol 95% about 900 Cc. with constant shaking. Dilute with Alcohol to 1000 Cc., mix and set aside until the oily drops of 'Aldehyde resin' have separated. Decant twice.—J.C.S.A. ii./08,689.

**Potassii Bromidum.**

**DETERMINATION OF CHLORIDE IN.**—In the Silver Nitrate titration method it is more accurate to add excess of silver nitrate and determine excess with standard sulphocyanide solution than to use potassium chromate. It is, however, better to oxidise the hydrobromic acid in acid solution with an oxidising agent, *e.g.*, ammonium persulphate or lead peroxide. The hydrochloric acid being unaffected by these can be titrated with silver nitrate solution. (Caspari, Meyer Bros. Drug, 1905,249.)

**Potassii Percarbonas.**  $K_2C_2O_6 \cdot H_2O = 216 \cdot 216$  I. Wts.

White crystals, soluble in water, giving off oxygen. Used chiefly as 'Anti-hypo' in photography, also for decolourising instead of Sulphuric Acid in Ziehl Neelsen's method of staining *Bacillus Tuberculosis*, *q.v.*

**Potassii Cyanidum.**

Potassium Cyanide  $\frac{1}{2}$  grain made into a Pill with soap or other 'floating' material and colouring matter for tinting water forms a good method of killing the larvæ of mosquitoes (*Culex pipiens*) in pools, 1 in 300,000 is said to kill in a few hours.—B.M.J. ii./11,712.

**Potassii Chloras.****Schulze's Maceration Mixture.**

A mixture of Potassium Chlorate 10 (moistened with water) with Nitric Acid 40 : or a Solution of 0.06 Potassium Chlorate in Water 100 Cc. and 1 Cc. of Nitric Acid. For separation of muscle fibre in animal, and ligneous tissue in vegetable histology.

**Potassii Metabisulphis**  $K_2SO_3 \cdot SO_2 = 222 \cdot 34$  I. Wts. FR. Cx.

Anhydrous Crystals soluble in 2 parts of water. Treated with acid it liberates about 52 to 57% Sulphurous Anhydride. (FR. Cx.).

Manufactured by passing Sulphurous Anhydride ( $SO_2$ ) into Potassium Carbonate until saturated. The metabisulphite is then precipitated with Alcohol. This salt has a similar action to ordinary sulphite in preserving Pyrogallie Acid from oxidation and preventing the staining of gelatin films. It has the drawback, however, that on oxidation free Sulphuric Acid is produced, requiring an extra amount of alkali to neutralise it.—(P.J.F. 1904). The Sodium Salt has analogous composition.

**PRUNI VIRGINIANÆ CORTEX.**

Identification of various Spurious Cherry Barks. *P. Avium* is paler; taste bitter and astringent. Almond odor scarcely perceptible. *P. Pennsylvanica*, red brown, taste scarcely bitter. *P. Virginiana*. The bitter almond flavour is more perceptible than in any except *P. Serotina*.—Holmes P.J. i./09,192.

The bark yields 0.075% of its weight HCN.—B.C.D. ii./09,131.

Chemical examination of a species of *Prunus*, said to be closely allied to *Prunus emarginata*. The constituents, amongst which is Prunetin, a new dihydric phenol  $C_{16}H_{12}O_5$ , appear to bear no relation to those known to be in *P. serotina*—this substitute for the genuine article differs in that when moistened with water there is no formation of Benzaldehyde and Hydrogen Cyanide as with the genuine bark.—P.J. ii./10,604.

**Syrupus Pruni Virginianæ.**

Hallaway finds the *Off.* method extracts 35%, Cline's 50%, Beringer's (with Glycerin), about 70% of the hydrocyanic acid. Glycerin extracts Tannin. Cline's process—which consists in macerating the bark 2 to 4 hours

at 60° C., then percolating, adding Glycerin to the percolate and finally dissolving the sugar, is thought best. This reduces the Tannin content and increases the HCN, the enzyme being more active at the higher temperature but even in the strongest syrup the HCN strength is only 0.008 per cent., or roughly 1/13, the strength of Cherry-Laurel Water.—P.J. 1./09,798.

It is recommended to modify the U.S. process by packing and macerating the moistened powder in a percolator 24 hours with water q.s. to submerge and to percolate until the receiver containing the Glycerin contains 600 Cc. of liquid at least. U.S. has a considerable error here.—Am. Jl.Ph. July /09,316.

## RADIOLOGY.

### Ultra-Violet Rays.

#### WATER STERILISATION.

Bacteria in water can be killed with remarkable speed by ultra-violet Rays. The Cooper Hewitt Apparatus provides 132 gallons of sterile water per hour.—L. ii./10,1784 gives particulars of experiments conducted with an improved type of the apparatus. With a flow of more than 600 cubic meters per 24 hours through the machine, and a consumption of less than 26 Watts per cubic metre, a content of 500 to 1,000 B. Coli per litre and total germs of 20 to 260 germs per cc. in the in-flow; the B. Coli were reduced to nil and the "germs" to practically nil in the out-flow. There would appear to be a wide and great future for this new system. It destroys both pathogenic and non-pathogenic organisms and all spores.

14 specimens of water treated by the ultra-violet rays were absolutely sterile.—L. ii./11,779; see also B.M.J. i./13,464.

The rays from the quartz-mercury lamp colour manganese glass violet within 12 hours. It is suggested that the mixture of Ferric and Manganous Silicate become changed into Ferrous and Manganic Silicate.—C.D. i./05,756; L. i./05,512.

On a method of producing ultra-violet rays by low tension high frequency currents.—L. i./06,587.

**Mercury Vapour Lamps**, violet and ultra-violet rays from, have considerable germicidal effect on an organism like *B. prodigiosus*.—Hewlett, L. i./09,743.

Milk can be sterilised by this means.—L. i./09,798.

The proportion of ultra violet Rays emitted by a given Lamp depend greatly on whether it is water-cooled or not and also upon the age of the lamps.—Na. July 1911, p. 102

The action of the ultra-violet Rays of the Mercury Lamp on *Citrate of Silver Paper* is parallel with the bactericidal action upon *Bacillus Coli* and the yield of such a lamp when used for sterilising purposes may be very conveniently controlled by such papers.—Na. Aug. 1811, p. 169.

A solution of Ammonium Nitrate under the action of ultra-violet light forms some Nitrite. The effects of ultra-violet light are generally similar to those of ferments.—Na. Mar 1911,68.

The ultra-violet radiation of the Mercury Lamp is more intense as the temperature of the luminous tube increases. For experiments in photo-chemistry the lamp may be relied upon as a constant source of ultra-violet rays, the radiation being defined when the voltage, ampèrage and length of tubes are known.—Na. Aug. 1911, 272.

The action of ultra-violet rays on certain toxic substances, Cobra venom is rapidly destroyed by exposure to these rays. Strophanthins have their activity markedly diminished by exposure to the rays for 30 to 120 minutes. Saponin completely loses its hæmolysing power after such exposure.—P.J. ii./11,779.

**Tungsten.** *Syn.* (German) Wolfram, W=184 I. Wts. With Uranium and Molybdenum forms the Molybdenum group of metals. Tungsten has been advocated to replace Platinum for electrical (*c.f.* Coolidge's Tungsten 'X' ray tubes, *Vol. I.*) and chemical work. It is more durable and cheaper.—B.M.J. ii./13,183.

## RHEI RADIX.

The active principle of rhubarb is a non-glucosidic resin. The anthraquinone derivatives previously stated to be active are entirely devoid of purgative action.—Tutin and Clewer, J.C.S. 1911,99,946; P.J. i./13,403



see also P.J. i./11,529; see also P.J. i./07,587. *Rheum Palmatum*, the source of Medicinal Rhubarb.—P.J. i./11,529.

According to P.G.V. should yield 35% extract on macerating 24 hours with a mixture of equal parts alcohol and water.

*Colorimetric Assay*.—All good rhubarbs containing from 2·8 to 4% of oxy-methyl-anthraquinones are said to comply with the test given in P.J. ii./05,580.

**POWDERED RHUBARB**, Standards suggested.—12 per cent. of ash on the air-dried drug, and 35 per cent. of extractive.—E. T. Brewis and H. Deane, P.J. ii./13,146.

## SACCHARUM.

Lumps of *Pure Cane Sugar* rubbed together in the dark produce luminosity.—B.M.J. i./11,752.

**Cane Sugar** may be (in the absence of a polarimeter) be approximately estimated by heating 1 Gm. of the same in 50 Cc. of water, to which 10 drops of hydrochloric acid have been added, for half an hour on a water bath. The solution is then cooled and neutralised with soda and made up to 100 Cc. with water, and the Invert Sugar thus formed is estimated with Fehling's Solution, 1 Cc. of which is approximately equivalent to 0·005 Gm. of Invert Sugar, the calculation being on the basis that 360 of Invert Sugar represent 342 of Cane Sugar.

Estimation.—A 10% solution at 20° has  $[a]_D = +66·486°$ .—P.J. ii./04,714.

Decomposition products of sugars as affected by various oxidising agents. Formic Acid, a very small quantity of acetaldehyde and apparently glycuronic acid formed.—L. ii./11,1418.

## SAPONES.

The following is the approximate composition of Pharmaceutical Soaps,—W. H. M.—B. & C. D. ii./94,575.

**Sapo Animalis, Curd Soap**. Principally Sodium Stearate; made with Sodium Hydroxide and a purified animal fat consisting principally of Stearin:—Fatty Acids 60%, Combined Alkali 9%, Uncombined Mineral Matter 2%, Water 30%. Limit test for Alkaline Hydroxide and Carbonate and free fatty acid are imposed for this and

**Sapo Durus (Hard Soap)**. Castile Soap is principally Sodium Oleate. Manufactured with Sodium Hydroxide and Olive Oil:—Fatty Acids 60%, Combined Alkali 8%, Uncombined Mineral Matter 2%, Water 30%. It is soluble about 1 in 20 in water.

**Sapo Medicatus**, P.G.V., Ph. Ned. (Full directions for making are given).

Genuine Olive Oil Castile Soap is greyish, while Cocoonut Oil Soap is pure white. Iodine No. is the best test.—C.D. i./07,869; i./08,523.

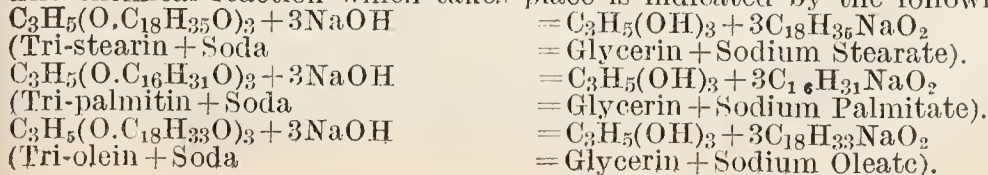
**White Castile Soap and Mottled Castile Soap** are trade varieties. Mottle is produced by adding iron or residues and scrapings of the lye tanks.

**Sapo Venetus** (Syn. *Savon de Venise*) similar to *Savon bleu ou Marbré* is a mottled Castile Soap.

**Sapo Mollis, Sapo Viridis, Soft Soap**, consists principally of Potassium Oleate. Manufactured from Potassium Hydroxide and Olive Oil:—Fatty Acids 45%, Combined Alkali 8 to 11% (reckoned as  $K_2O$ ), Insoluble Mineral Matter 1·0%, Water 35 to 45%, Matter insoluble in Alcohol 3% allowed (*i.e.* Potassium Carbonate and Insoluble Soaps).

In soap-boiling caustic soda of high purity, 96-98%, is used for the best varieties. The lye employed (into which the melted fat is poured) has Sp. Gr. 1·075. Boiling proceeds with occasional further addition of lye.

The chemical reaction which takes place is indicated by the following:—



The soap thus produced is salted out with salt, and the glycerin formed is recovered as much as possible from the spent liquor. It is essential to ensure that the fats have been thoroughly saponified, as also that no marked excess of alkali is introduced. The next step is to clarify the soap by boiling with a fresh supply of water from any insoluble soaps, *e.g.*, Lime and Magnesium Salts of the acids indicated above. The "nigre" containing these impurities subsides in this manner to the bottom of the vessel. The soap is then allowed to slowly cool and "settle." When cooled to 165° F. it is removed to the frames to solidify. Here it remains for a month to consolidate, and drain through apertures in the sides of the containing vessel.

For **Household Purposes** this soap is then cut up with wires into bar form and stamped.

For **Toilet Purposes** special soap bases are employed containing a large proportion of stearates (obtained from 'edible' animal fats—tallow). It is obvious that the fats must not be rancid or of strong colour. A high acidity and unpleasant odour would render the fat quite inadmissible. A proportion of palm oil is generally combined with the tallow.

The soap ultimately is converted by special machinery into ribbon-shaped shreds, it is perfumed and after other treatment is finally stamped in moulds—*vide* xivth edition for further details.

For **Shaving Soap** it is necessary to employ fats—'strong' tallow—with a high melting point.

Ordinary Household soaps are made with vegetable oils of light gravity.

Good average soap can be produced by saponifying vegetable oils, such as those of Cottonseed, Palm, or Cocconut (of this the best variety is known as "White Cochin" Oil, the second as "Ceylon" Oil); but these oils containing a large proportion of the Oleic Ester produce more soluble, *i.e.*, wasteful soaps.

The use of **Resin** in household soap is not at all injurious; on the contrary resin soap is very soluble and lathers freely. The addition of the resin renders the soap smooth and prevents efflorescence. Further, the cleansing 'odour' imparted by the resin is appreciated. It is not, however, suitable for toilet purposes, and a large admixture cannot be allowed. Occasional additions to common soaps are chlorophyll, sodium silicate and French Chalk.

**Transparent Soaps** are made by setting from methylated spirit. Many contain resin and sugar (as much as 20% of each).

In Germany manufacturers have the privilege of using pure spirit with 1 Kilo of Castor Oil and 400 Cc. of Soda Solution per 100 litres of Spirit to 'denature'—C.D. ii./o6,718. It is stated that in the manufacture of transparent soap with methylated spirit only about  $\frac{1}{2}$  the spirit is recovered—the rest is lost in drying.

**Toilet Soaps.**—Examination of a large number showed little adulteration. Free *alkali* is comparatively rare.

The **Valenta figure** records the temperature at which a mixture of equal volumes of Acetic Acid and Fatty Acid result in a uniformly clear and bright solution. The majority of the figures obtained and melting points, *etc.*, approach those of Palm and Cocoa Nut Oils.—L. i./14,52.

### Saponification Equivalents of Fats and Oils.

The *Saponification Number* or Köttstorfer's Number is the number of milligrammes of Caustic Potash which the fatty acids contained in 1 Gm. of the fat (free from moisture) are capable of neutralising. To 1.5 to 2.0 Gm. of the purified and filtered specimen for examination contained in an Erlenmeyer flask of about 200 Cc. capacity add 25 Cc. of N/2 Alcoholic Caustic Potash. Warm half an hour on water-bath with reflux condenser, with occasional rotation, add a little phenolphthalein solution and titrate excess of alkali with N/2 Hydrochloric Acid. Conduct a control using the alkali alone.

The difference in the number of Cc. of N/2 Hydrochloric Acid required to neutralise in the control and the actual test is converted into the number of mgr. of KOH consumed by the amount of the fat or oil originally taken and the result is expressed in equivalent of 1 Gm. of the specimen.



**Some Saponification Numbers:—**

Adeps 195—203.	Oleum Lini 187—195.
Adeps Lanæ 90—102.	Oleum Morrhuæ 175—185.
Oleum Adipis (U.S.) 195—197.	Oleum Olivæ 191—195.
Oleum Amygdalæ 191—200.	Oleum Ricini 179—180.
Oleum Gossypii Seminis.	Oleum Theobromatis 188—195.
191—196.	Oleum Tigllii 212—218.

Solution of Potash in Propyl Alcohol suggested to replace Potash in ordinary Alcohol.—P.J. ii./11,9.

For Iodine Number of Fats, *see* p. 74.

**SCAMMONIÆ RESINA.**

In the testing of Scammony Resin for complete solubility in ether the presence of water in the ether makes a considerable difference. A Soxhlet is not recommended. It is best to macerate 6 hours 3 to 4 Gm. of the resin finely powdered in 30—40 Cc. of ether in a short, wide-mouth flask. Filter off and weigh insoluble matter and give percentage on the dry resin.

Solubility in 0.720 Ether, Acid and Saponification Values, also tests for Colophony, Guaiacum, etc.—P.J. ii./08,365.

Saponification Values characteristic of both the resins—of *C. Scammonia* and *Ipomœa Orizabensis*—enables detection of the Mexican Scammony. In the case of the former the Saponification No. is in the neighbourhood of 238, and in that of the latter a little below 190. For quantities and method of work consult Am. Jl. Ph. Mar. '09, p. 105. *See* also P.J. i./12,285.

A spurious sample made of brown industrial resin admixed with fine powdered Scammony Resin.—C.D. ii./11,897.

Scammony Resin is now a mixture of resins from Scammony root or from Orizaba Jalap root. *Ipomœa Radix. Off.* (*Ipomœa Orizabensis*), entirely soluble in Alcohol (90%). Not less than 75% soluble in ether. Tests are given for absence of certain foreign resins, especially Colophony.

**SENNÆ FOLIA.**

**Senna Leaf Constituents.**—An examination of Tinnevely leaves, leaves grown at Lima (botanically identical) and Alexandrian leaves, yielded (1) Salicylic Acid (not previously noted as a constituent), (2) Rhein  $C_{15}H_8O_6$ , previously only known as a constituent of rhubarb, (3) Kæmpferol, (4) Aloe-Emodin and other bodies. The purgative action is in part due to the Aloe-Emodin,—and other bodies.—F. Tutin, P.J. ii./13,741; C.D. ii./13,743.

**Powdered Senna.**—20 samples found free from actual adulteration, but some of them had been made from low-grade material, as shown by the absence of green colour and the presence of stalks and sand. Easy for the pharmacist to determine the quality of senna powder microscopically.—Prof. Greenish, P.J. i./13,365,370.

**SINAPIS SEMINA.**

**Black Mustard** contains the glucoside Sinigrin, this is—

Potassium Myronate =  $C_{10}H_{18}KNS_2O_{10}$  = 415.394 I. Wts. with Myrosin, which is similar to the ferment Emulsin in Bitter Almonds. This glucoside splits up under the influence of water with evolution of Allyl-iso-sulphocyanate,  $-C_3H_5NCS.$  = 99.12 I. Wts., the principal constituent of the Essential Oil. P.G. requires Black Mustard Seeds to yield at least 0.7% of this.

**White Mustard Seeds** contain the glucoside Sinalbin  $C_{39}H_{44}N_2S_2O_{16}$  = 752.512 I. Wts.

This also splits up with water and Myrosin with evolution of an oil, White Mustard Oil (acrinyl isothiocyanate)  $C_6H_4OH \cdot CH_2 \cdot NCS$  (1:4) = 165.136 I. Wts., which, however, cannot be distilled with water. As the black seeds contain an excess of their glucoside and the white an excess of the ferment, the combination of the two produces the strongest effect. Some work by Prof. Greenish recently, however (P.J. i./12,203), shows that in all the samples of black mustard-seed examined—both old and new—there was sufficient myrosin to decompose all the sinigrin present, and that properly preserved black mustard-seeds retain their myrosin unimpaired for many years. Two samples examined contained sufficient myrosin to decompose a much larger quantity of sinigrin than the seeds themselves contained.

The percentage of oil is 0·3 to 0·86. Dutch Seeds are best. Examination, Detection of Myrosin and Sinigrin.—P.J. ii./04,475; i./05,719.

**Oleum Sinapis Volatile.** The following tests are now given *Off.*—Sp. Gr., 1·014 to 1·025. Distils between 148° and 156° C. Should contain not less than 92 per cent. of allyl-iso-thiocyanate, determined by a process provided.

Synthetic Oil might be allowed.—P.J. ii./10,437.

## SODIUM.

An electrified gas from *Sodium*, according to C.E.S. Philips, exists which discharges a negatively charged electroscope: not so much when + charged. This is *not* due to rapid oxidation of the surface of the Sodium. Na., May 28, '08, 79; June 11, '08, 127.

### Bismuth-Cæsium-Potassium Nitrite.

Dissolve 50 Gm. of Potassium Nitrite in 100 Cc. of Water, neutralise with Nitric Acid and add 10 Gm. of powdered Bismuth Nitrate, then add sufficiency of 10% solution of Cæsium Nitrate to precipitate the Sodium present in the Potassium Nitrate, filter and add Cæsium Nitrate to a total of 2·5 Gm.

A reagent by means of which small amounts of Sodium may be detected and estimated in presence of large quantities of potassium, the corresponding Sodium Salt 5 Bi (NO<sub>3</sub>)<sub>3</sub>·9Cs.NO<sub>2</sub>·6NaNO<sub>2</sub> being almost insoluble.—Nature, Feb. 24, 1900, p. 498.

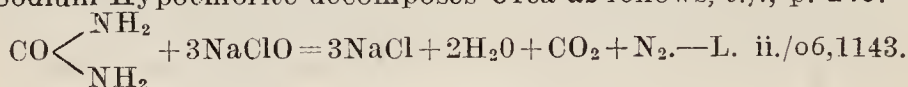
A slightly varied formula for the Sodium Salt is stated—also that 1 of Sodium Nitrite in 3000 of Potassium Nitrite can be detected by the reaction.—P J i./13,673. The amounts of the ingredients in the proportions stated in the "Nature" reference show an excess of Potassium Nitrite and Bismuth Nitrate over the amounts required theoretically,—these would be 51 Potassium Nitrite, 48 (Crystalline) Bismuth Nitrate and 39 Cæsium Nitrate.

**Liquor Sodæ Chlorinatæ** (*Off.*). *Syn.* Eau de Javelle. 2·5% Cl. U.S. 2·4%. *Dose.*—10 to 20 minims. Dissolve Sodium Carbonate 600 in Water 1,000. Triturate Chlorinated Lime 400, with Water 3,000. Mix, and filter. U.S. employs Monohydrated Sodium Carbonate 65, Chlorinated Lime 90, Water to 1,000. Process slightly modified.

*Should be freshly made.* Other Pharmacopœias use more Sodium Carbonate to obtain a preparation which will keep better.

For estimating Urea in urine, Sodium Hypobromite we found is *more accurate*,—the Nitrogen being evolved more rapidly and completely.

Sodium Hypochlorite decomposes Urea as follows, *c.f.*, p. 249.



### Water Sterilisation with Chlorine.

Nesfield found 0·125 Gm. Chlorine per litre (125 per million) in water teeming with *B. Typhosus*, *B. Coli*, etc., sufficient to sterilise it in 5 minutes. Description of principle of Nesfield's Sterilising Tablets.—L. ii./08,1708. One of Chlorine in 1,000,000 of Water acting 15 minutes will kill cholera vibrio in it.—L. ii./10,1213. *c.f. also Calx Chlorinata*, Vol. I., p. 234.

**Sodium, Ammonium and Potassium Persulphates**, are strong bleaching agents, the latter K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>=270·34 l. Wts., known as **Anthion**, and the Ammonium Salt are used in Photography to reduce dense negatives—they oxidise and then dissolve part of the silver.

On adding Barium Chloride to a solution of Potassium Persulphate there is no precipitation, but on warming, Barium Sulphate is thrown down.

The Ammonium Salt (NH<sub>4</sub>)<sub>2</sub>S<sub>2</sub>O<sub>8</sub>=228·224 l. Wts. is prepared by electrolysis of a solution of ammonium sulphate containing sulphuric acid. In presence of water it yields ozonized oxygen. To sterilise sponges. It has been used as a hand disinfectant. It bleaches.

For details of the therapeutic use of the Sodium Salt, see Vol. I.

### SEPARATION OF CHROMIUM, IRON and ALUMINIUM by means of AMMONIUM PERSULPHATE.

The precipitated hydroxides are mixed with water in a porcelain capsule, a small quantity of ammonium persulphate is added and the dish warmed until



the precipitate is dissolved. Thus the chromic hydroxide is converted into a compound of chromic anhydride. On the addition of an alkali the iron is precipitated as a ferric hydroxide and the aluminium and chromium can be detected in the solution in the ordinary way. Re-solution of the ferric hydroxide in acid and reprecipitation with alkali effects a complete separation of the iron.—C.D. i./11,133.

### Sodii Hyposulphis.

Hampshire and Pratt find that semi and decinormal solutions decomposed slightly but even after 8 months these dilute solutions are reliable for volumetric work. The deposit of Sulphur may be due to oxidation or action of  $\text{CO}_2$  or to a simple decomposition by light.—P.J. ii./13,142.

To preserve the volumetric solution of Sodium Thio-sulphate a few drops of carbon disulphide added are useful.

**Spiritus Ætheris Nitrosi, see Ætheris Nitrosi Spiritus.**

## STROPHANTHUS.

Experiments on removing fat from, by cooling to  $14^\circ \text{C}$ , and by other methods. Cooling satisfactory.—P.J. ii./99,469.

It has been stated that the fat in Strophanthus Tincture gives it an emetic action. Experiments on animals in America show this to be unfounded,—the fat being void of action. On the other hand, a dose of fat-free tincture injected *subcutaneously* produced prompt emesis.

In making the tincture it is important to employ *slow* extraction (by 65% Alcohol) in a long narrow percolator. A lower percentage Alcohol extracts the active principle more rapidly, producing an unsightly tincture which may be cleared by chilling and filtering in the cold. Defatting the seeds aids percolation but does not affect the strength of the tincture. When making in small quantities percolate at least 7 days with 1000 Cc. of Menstruum for each 100 Gm. of seeds. In addition there should be several periods of exhaustion of at least 8 hours each. Suggested min. lethal dose of the tincture  $\frac{1}{30}$  to  $\frac{1}{15}$  Cc per kilo of cat, injected subcutaneously (*i.e.*, about 40 cat units per Cc.). The seeds should be standardised to start with, *i.e.*, of the strength indicated by about 400 cat units per Gm. of seed.—Am. Jl. Ph., May, '09,209.

### STROPHANTHUS SEEDS. THEIR ASSAY BY CHEMICAL METHODS.

The powdered seeds (20 Gm.) are freed from oil by percolation with Petroleum Ether or Ethyl Ether,—they are then exhausted with Alcohol 70%. This tincture is evaporated to a soft extract at a low temperature, dissolved in 100 Cc. of Water, filtered in a separator, 3.2 Cc. of Sulphuric Acid (25%) added, then shaken out thrice with 20 Cc. Ether. The aqueous acid solution is warmed in a water bath for one hour at not exceeding  $75^\circ \text{C}$ . This decomposes the Strophanthin present into Strophanthidin and Strophanthobiose Methyl Ether. It is then cooled and shaken out in a separator with 10 Cc. of Chloroform,—Strophanthidin being soluble in this reagent. This is evaporated to a low bulk in a tared dish, allowed to crystallise out and dried at below  $65^\circ \text{C}$ . The result divided by the factor 0.365 gives amount of Strophanthin present. Various samples of the seed by this method gave 3.1 to 4.57% Strophanthin. A standard of 0.1% w/v Strophanthin is suggested. A chemical method is probably as useful as the physiological test.—J. Haycock, P.J. i./11,553; B.C.D. i./11,94.

**Fromme's 1910 Assay Method.**—In a critical comparison by J. B. Lampart and A. Muller, of various methods of assaying Strophanthus Seeds and Tincture, including Fraser's, Fromme's 1897, 1900, 1905 and 1910, Thom's, Mann's, Dohme's, Haycock's, Dowzard's and Barclay's. Fromme's 1910 method was found to give best results and to agree well with physiological results. It is as follows:—7 Gm. of seeds finely powdered are boiled one hour with 70 Gm. of Absolute Alcohol in a tared Erlenmeyer flask (200 Cc.) under a reflux condenser. It is then cooled and made up to original weight with Absolute Alcohol. The liquid is filtered and 50.5 Cc. (=5 Gm. seeds) of this evaporated on a water-bath, the residue being extracted with Petroleum Ether to remove fat. The undissolved portion on the filter is washed back into the dish with 5 to 8 Gm. of boiling water. The whole is heated to boiling and 5 drops of Lead Acetate Solution and 0.2 Gm. of Kieselguhr are

added, the whole mixed and transferred to a 5 Cm. filter and filtered into a 100 Cc. Erlenmeyer flask, washing through with boiling water in small quantities until the washings are no longer bitter.

Five drops of Hydrochloric Acid are added to the filtrate which is then boiled gently for two hours. It is then made up to 20 Cc., cooled and extracted with two quantities of 10 Cc. of Chloroform which are filtered into a 100 Cc. flask. The aqueous portion is boiled again for half an hour, extracted with Chloroform as before and if the aqueous portion is still bitter the process must be repeated. The mixed Chloroformic Extract is distilled, the residue dried in desiccator to constant weight. This consists of Strophanthidin, and when multiplied by 2.187 gives the weight of Strophanthin represented.

For the **Tincture** 51 Gm. is evaporated, the residue is dissolved in 20 Gm. of hot water, 20 drops of lead Acetate Solution and 0.2 Gm. of Kieselguhr are added and the process continued as above.—W. Kroseberg, P.J. i./14,590.

### TEREBINTHINA CANADENSIS (*Off.*), U.S.

The balsam obtained from *Abies balsamea* (*Coniferae*), known as Canada Balsam. Is a constituent of Collodium Flexile (*Off.*). It has a refractive index approximating that of microscopic glass, and 'sets' in a non-crystalline transparent condition, hence is used as a mounting medium. In preparing for use it has to be gently heated in an open dish for a week or more until a small quantity removed becomes brittle when placed on a cold slab. Canada Balsam 1 part by weight in Xylol, in turpentine, in benzol, and in chloroform, each 1 by measure, are prepared for microscopic use. The first mentioned is chiefly employed and is frequently designated '**Xylol-Balsam.**'

Canada Balsam contains 18 to 20% of oil. For adulterants and table of composition of this and other coniferous resins, *vide* Allen, 1911, Vol. IV., p. 79.

### THALLIUM.

Tl=204 (I. Wts.)

This element, resembling lead on the one hand and Potassium on the other, was discovered by Crookes by spectral analysis in residues of sulphuric acid manufacture.

Thallium Acetate  $Tl\ C_2H_3O_2 = 263.024$  (I. Wts.). *Dose.*— $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 Gm.) was tried in syphilis, but is not equal to mercurials; if given an hour before the commencement of a sweat, was found of value in the night sweats of phthisis. Loss of hair and arrest of perspiration accompany its use.

**Poisoning by Thallium Acetate.**—A workman drank a small quantity—less than 1 Gm. in solution in a Vichy bottle. Caused vomiting, acute sense of internal chill, cyanosis, lowered temperature, pain in the kidneys and reduction in urine voided. Abundant drinks were ordered, and baths. Symptoms disappeared in a few days. Loss of hair and arrest of perspiration were *not* seen.—L. i./II, 1461.

### THEOBROMA.

**Theobroma Oil, Detection of Adulteration.**—An authentic specimen has following characters:—S.V. 196, I.V. 31, Volatile Fatty Acids 0.7%, Acid Value 0.6, M.Pt. 27° C. Butyrorefractometer reading at 40° C. 46.5. Soluble in Ether 1 in 2, clear at 18° C. Coconut fat, Wax, Spermaceti, Margarine and Paraffin must be searched for.—Y.B.P., 1913, 97.

'**Cocoa.**'—The ground nibs of Theobroma Cacao from which most of the fat has been removed.

At the second International Food Congress (1909) it was declared that the use of alkali should be tolerated—the whole question being submitted to an international commission. The use of alkali enables the production of a "cheap" cocoa.

The examination of a number of Cocoas on the market showed moisture to range from 3 to 8%, Nitrogenous Matter ( $N \times 6.3$ ) 19% to 20%, Fat 26 to 31%, Mineral Matter 3.9 to 8.8%, Theobromine 1.7 to 2.0%.—L. i./05, 316.

**Health and Strength Cocoa** (\*Sandow's) differs from most in having its nitrogenous constituents increased by further elimination of fat and a special method of preparation produces the cocoa in a very finely powdered condition.—L. ii./II, 1493.



M.P.C. on the other hand says: According to analysis it is "a much of muchness with most of the cocoas on the market."

The nitrogenous constituents have been slightly raised above the average but this has been done at the expense of the fat. Compared with the ordinary milk cocoas and milk chocolates, it contains about only half the total nitrogenous constituents that are found in the latter.—M.P.C. ii./11,411.

The generality of the Cocoas made by Manufacturers of repute and sold on the English market do not contain alkali. There has been some misconception on the part of some people in interpreting results of analysis. Clearly the natural salts of Cocoa yield alkaline Carbonate on ignition. That sold by E. Sandow yields alkalinity of ash equivalent to 2.82%  $K_2O$  which is as high as most of the cocoas examined by the "*Lancet*." In some cases alkali is used in the preparation of Cocoa, but false alarms should not be raised. The presence of true alkali—caustic alkalis—in cocoa is inconceivable.—L. i./13, 258.

A certain cocoa is guaranteed to contain no starch when in fact it is present. E. J. Parry, P.M.C.E., C.D. i./13,562.

**Essential Oil of Cocoa** 12 Gm. obtained from 1000 kilos of beans by distilling at  $120^{\circ}C$ . with superheated steam. The Oil, resembling Coriander somewhat, has an intense odour, being perceptible in 1 in 50,000,000 of Syrup.—C.D. ii./12,752.

## ANIMAL ORGANOTHERAPY.

### SUPRARENAL CAPSULES.

The maximum effect is produced by intravenous injection of  $\frac{1}{120}$  grain (0.00054 Gm.) of the dry extract per 2½ pounds (1 kilogramme) of body weight,  $\frac{1}{8000}$  grain (0.00008 Gm.) has a distinct action on the heart and arteries of an adult.—B.M.J. ii./02,170.

**Colorimetric and Physiological estimation of the active principle of the Suprarenal Gland.**

The following method is said to have given satisfactory results:—

With samples containing 0.2—0.8% of the active principle 0.01 Gm. is placed in a test tube with 5 Cc. of dilute Hydrochloric Acid (2.5 Cc. N/10 Hydrochloric Acid per 100 Cc.) and 5 Cc. of 0.2% Potassium Iodate Solution, the mixture heated just to boiling point and allowed to stand 15 minutes; it is then filtered and the colour compared with a series of standards corresponding to 0.01 to 0.10 mgr. per 10 Cc. The best physiological method consists of the determination of the relative rise in blood pressure in dogs as compared with a given amount of the pure base.—Am. Jl. Ph. Dec. 1911, p 551

### Adrenalin.

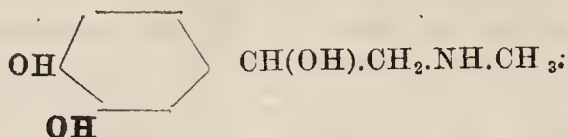
**TEST OF IDENTITY.**—A peculiar odour like phosphoretted hydrogen is developed on treating a small quantity of the salt or solution with a few drops of sodium hydrate solution.—P.J. i./07,718,774,797. See also Organic Analysis Chart.

**Epinephrin.**—J. J. Abel isolated Epinephrin. This is capable of producing a prolonged rise in blood pressure when introduced into the circulation. The effect on respiration is at first excitant, but later paralysing through its action on nerve centres, while the heart is only paralysed with difficulty and after repeated doses.—M.P. Oct. 20/09,413.

Abel showed that Adrenalin of Takamine is not chemically pure. Aldrich, Abel's former associate, obtained an extremely pure form of the body and retained Takamine's name, but its production by Aldrich's method is not commercially possible. This Adrenalin and Abel's later product, Epinephrin, are probably identical.—Am. Jl. Ph., July/08,323.

P. May summarises the matter as follows:—The active principle of the suprarenal gland was first obtained in an impure condition by Abel and Crawford in 1897, and in a more pure condition as the Benzoyl derivative in 1899. They called it Epinephrine, and it was also isolated by v. Fürth who called it Suprarenine. Takamine (1901) first obtained it crystalline and gave it the name Adrenalin. Shortly afterwards it was isolated by Aldrich by a somewhat different method and given the formula  $C_9H_{13}O_3N$  (as above stated) which is now universally adopted. After other suggestions Jowett confirmed the

formula of Aldrich and Friedman and aided in clearing up the constitutional arrangement as



See also L. i./II, 400.

It would appear that the pancreas has the power of inhibiting the sensitiveness to Adrenalin in certain organs supplied by the sympathetic nerve—i.e., normally Adrenalin does not dilate the pupil, but this does occur in certain cases, e.g., extirpation of the pancreas, pancreatic insufficiency, in diabetes, and in some cases of Basedow's disease. This susceptibility is probably due to hyperthyroidism.—J.C.S.A., ii./08, 712.

Effect produced on tracings in counteracting Epinephrin action with Nitroglycerin.—Martin, C.D., ii./09, 213.

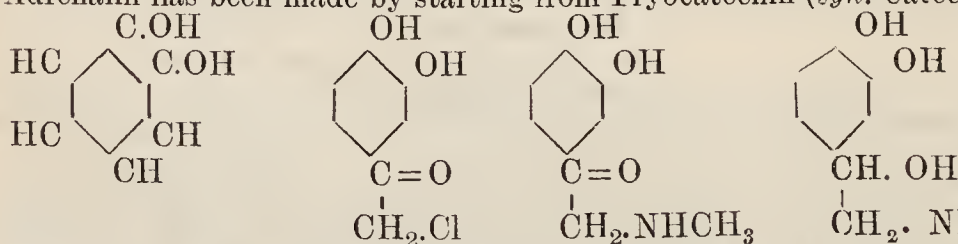
There is some doubt as to the **Amino-Acid** from which Adrenalin is built up, but the chemical constitution of **Tyrosin** and Adrenalin is sufficiently close to be very suggestive. It is known that the action of bacteria on Tyrosin results in its splitting up and this fact may explain some of the symptoms of intestinal stasis. The abnormal presence of bacteria in the small intestine results in a decomposition of the Tyrosin which is, therefore, absorbed in deficient amount and consequently the suprarenal gland being supplied with a deficiency of the precursor of Adrenalin is able to manufacture only a deficient amount and a deficiency of Adrenalin proportionate to the amount of intestinal infection, with the corresponding symptoms, results.—From a Paper on Intestinal Stasis.—L. ii./12, 1783.

**Mydriatic Power of Adrenalin.** The eye of the frog is so sensitive to Adrenalin that it may be used to detect minimal amounts of the substance. The mydriasis is observed in all conditions associated with increased excitability of the sympathetic system. May be used (instillation of the 1 in 1,000 solution) as diagnostic—though uncertain and inconstant. Functional disturbance of the pancreas, overaction of the thyroid, diabetes mellitus and perhaps exophthalmic goitre are associated with increased sensibility to Adrenalin. In all these states probably the adrenal content of the blood is increased.—B.M.J. i./13, 572.

Adrenine (Epinephrine) is present in the suprarenal glands of the whale, and can be separated from them, preserved in Chloroform after 6 to 9 months. Highest yield was 0.2% of the moist material, or about 1.2 Gm. from each gland.—Y. B. P., 1913, 2.

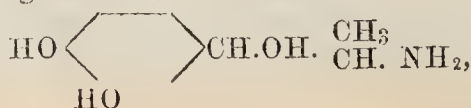
### **Suprarenin (Synthetic).** (See also Vol. I. p. 950).

A body with chemical and physiological properties very similar to those of Adrenalin has been made by starting from Pyrocatechin (*syn.* Catechol):—



converting this into Chlor-acetyl-pyrocatechin; thence with Methylamine into the Ketone (*syn.* Adrenalone), Stolz. Ber. 39 (1904) 4,149; D.R.P. 152, 814; English Patent (1903) 25,480; finally reducing to the body Dihydroxy-phenylmethylaminomethyl-Carbinol of the fourth formula above strongly resembling Adrenalin (by electrolytic reduction or by action of Aluminium Amalgam on the sparingly soluble sulphate of the Ketone.—D.R.P. 157,300). The Ketone is not much more powerful than the Chlor-acetyl body. They are both physiologically very active, but not nearly so powerful as the ultimate body.—Dakin, Jl. Physiol., Vol. XXXII. lii./05, 341. See also Jowett, P.J. i./05, 909.

A method of preparing a base of the formula





having similar properties to the active principle of suprarenal glands, has been patented. English Patent (1912), No. 8957. The process is to reduce  $\alpha$ -aminopropionylpyrocatechin with hydrogen in the presence of colloidal palladium and to separate the dextro- and lævo- compounds by means of dextro- and lævo- tartaric acids. The lævo- base has M.Pt.  $218^{\circ}$  C.; the dextro-base melts at  $217^{\circ}$  C.

### LIQUOR THYROIDEI.

**Assay.**—The author suggests as standard 0.025 Gm. Iodine in organic combination in 100 Cc. of Liquor—this being based on an average content in the fresh gland of 0.04%, the weight of the gland as at least 60 grains. The method of estimation should be to employ 10 Cc. of the Liquor and determine Iodine content on the lines of the process for Thyroideum Siccum.—*q.v.*

With the object of standardising Liquor Thyroidei (B.P., 1898), as to Iodine content, we assayed initially a Liquor a few months old. This Liquor had been prepared from thyroids which had not been previously assayed in the fresh condition—the object of this initial experiment being to ascertain any indication of Iodine content in the Liquor. 10 Cc. were treated with 2 Gm. of crushed Sodium Hydrate, incinerated and proceeded with otherwise exactly as under the Assay Process (W. H. Martindale's) for Dry Thyroid. This amount required 3.5 Cc. and 3.1 Cc. of N/100 Sodium Thiosulphate on two separate trials, showing a mean content of 0.042% Iodine. 100 minims of the B.P. 1898, Liquor are made to equal 1 entire gland, i.e., a weight of fresh gland of about 70 grains, and the Iodine content in the fresh glands in question was probably in the neighbourhood of at least 0.06%.

Following on this experiment, in March 1912 we prepared a quantity of Liquor Thyroidei from some fresh Thyroid glands which were assayed and found to contain 0.063% Iodine. The Liquor contained 0.015% Iodine. This indicated that about 45% of the total Iodine had been extracted by the process. The Dry Thyroid from these glands contained 0.24% Iodine (1 of the Dry preparation was yielded by 3.82 of fresh gland). The average weight of the lobes of these glands was only  $23\frac{1}{2}$  grains. It would therefore seem desirable that the Liquor formula should be altered so that a specified volume should be made equivalent to *weight* of gland and be finally standardised to 0.025% organically combined Iodine.

### THYROIDEUM SICCUM.

#### Assay of Iodine in Thyroid Preparations.

*Suggested standard 0.2% Iodine in Organic Combination.*

In our last Edition we provided a large amount of experimental data on the estimation of Organic Iodine in Thyroid Gland preparations. We described the various methods suggested by others and pointed out the *Sources of Error* in some processes which may account to a loss of even 25 to 50%. We devised a process which has given good results. It is as follows. (We must refer those requiring the antecedent experimental information to Edn. XV., Vol. II., p. 109).

**W. H. Martindale's Process.**

Weigh 2 Gm. of the Dry Thyroid, mix most intimately with 2 Gm. of crushed Sodium Hydrate in a small glass mortar to produce a uniform powder. Heat in a porcelain crucible about 5 Cm. in diameter until the mixture becomes uniformly grey. Allow to cool. Scrape out the ash carefully into the same mortar, reduce to fine powder, mix intimately with 1 Gm. of powdered Potassium Nitrate; transfer to the crucible, heat over Bunsen flame until white or almost so (blowpipe is not necessary on either occasion). Dissolve the flux in about 50 Cc. of Water. Place the solution in a separator, add about 30 Cc. of Petroleum Ether, and then carefully sufficient 25% Sulphuric Acid in portions to render distinctly acid to litmus paper—shaking slightly with each addition so as to “catch” the Iodine in the solvent as it is liberated. After thorough shaking remove the aqueous layer and repeat the extraction with about 20 Cc. Petroleum Ether and a drop or two of 10% Sodium Nitrite Solution. Combine the Petroleum Ether Liquors, wash with water and titrate with N/500 Thiosulphate. (Note.—For 2 Gm. of a 0.2% preparation about 14 to 16 Cc. of Thiosulphate Solution will be required,—the addition of the Sodium Nitrite Solution is not really necessary).

By this process a dummy of albumen containing 0.2% Iodine gave an average of 0.195% on four determinations.

Commercial samples of Dry Thyroid showed remarkable variation. They gave the following average percentages of Iodine :—

No. 1. 0.029%.	No. 4. 0.387%.
No. 2. 0.149%.	No. 5. 0.082%.
No. 3. 0.514%.	

It is certain the Iodine content in Thyroid Glands varies in different countries and at different seasons. The No. 3 we may mention came from two Provinces in Holland, and may be deemed exceptional. They were actual sheep's glands (not pigs'). It is just possible their feeding by the sea-shore had something to do with the remarkable content. The 0.514% in the dry gland would equal 0.1% Iodine in the fresh gland. The time of year (July) would also affect the yield. Since these assays were conducted, in March 1912, we found 0.063% Iodine in fresh glands from the same source and 0.24% Iodine in Dried Thyroid Glands from same (1 part of Dry Thyroid was = 3.82 of fresh gland). The average weight of the lobes of these glands was  $23\frac{1}{2}$  grains—they varied enormously—from 15 to 90 grains.

Further, we obtained the thyroids from a number of **English South Down Sheep** (bred near Southampton) slaughtered in January 1912—these glands may therefore be considered as a typical winter collection. The fresh substance yielded 25% Thyroideum Siccum (*i.e.*, 1 = 4 of fresh gland). The weight of glands was taken within two hours of slaughtering, hence there was no appreciable loss of natural moisture. On assay by our process we found the dried powder to contain 0.368% Iodine which is equivalent to 0.092% Iodine in the fresh gland. It will be noticed that these



glands were apparently drier than our summer supply—whether this is due to season or locality is open to discussion.

A paper by S. P. Beebe in the New York Med. Jl. 8/7/11, v. *infra*, gives the content of Iodine in mgr. per Gm. of fresh substance from sheep as from 0.006 to 0.415, i.e., 0.0006 to 0.0415% or from 0.003 to 0.2% Iodine on the dry gland approximately. This is a remarkable variation. Pigs' glands are stated to contain more,—

*viz.* 0.0084 to 0.288% in the fresh glands.

Ox Glands 0.003 to 0.147% in the fresh glands.

Human Glands 0.006 to 0.08% in the fresh glands.

See also T. B. Aldrich, J.C.S.A. ii./12, 1192. Results in Europe with regard to sheep seem therefore to be better than in the United States.

It is well known that the activity of Thyroid preparations varies greatly. This is quite likely due directly to their varied Iodine content. In view of the fact that Iodine content may be taken to indicate the amount of therapeutic activity it seems desirable to decide upon a reliable process of estimation and fix a standard,—we suggest as *standard* 0.2% **Iodine in Organic Combination** (with a test to exclude Inorganic Iodine.—*c.f.* U.S.P.)

*Note.*—‘The activity’ of the thyroid gland has been attributed to thyro globulin, an albuminous substance containing Iodine—the percentage of Iodine may therefore be a measure of the activity of a thyroid preparation provided the glands have not been subjected to any treatment that would cause alteration in this substance. B.M.J. i./10, 1242.

### References.

U.S. Pharmacopœial Standard for Desiccated Thyroid Glands. A close relationship has almost invariably been found between the Iodine content and the physiological activity of Desiccated Thyroid Gland.—Am. Jl. Ph., Sept. 1911, pp. 407—411.

The **Baumann Method** of assay consists in fusing with Caustic Alkali, liberating the Iodine, extracting with immiscible solvent and estimating colorimetrically. The **Hunter** method differs from this in using Alkali Carbonate for fusing; conversion of the Iodine into Iodate and estimating its amount by a volumetric procedure.—Hunter, Jl. Biol. Chem. 7, 321, 1910.

A number of Assays by Hunter's method showed an average yield in recent samples of American Dry Thyroid to be 0.2% approximately. This is suggested as Standard for U.S. with a latitude of 0.03%, i.e., the standard would be 0.17 to 0.23%.—Reid Hunt & Atherton Seidell.—Am. Jl. Ph., Sept. 1911, pp. 407—411.

The thyroid and parathyroid glands are entirely distinct (*q.v.* Vol. II.). The parathyroid contains no trace of Iodine.

The functional capacity of the thyroid is very nearly if not quite, in direct proportion to its content of Iodine. The Iodine contents in milligrammes per gramme of fresh gland from the *pig*, *sheep*, *ox*, etc., mentioned in this paper are stated above in our monograph on the Assay.

Iodine is thought to be contained in the thyroid as di-iodotyrosin, but there is uncertainty as to this. Iodothyreine is generally prepared by the hydrolytic action of some mineral acid or by digesting glands with Hydrochloric Acid and Pepsin—the substance however, is not a definite one like Adrenalin. Clinical results show that thyroid administered by the mouth is efficacious and that a very small quantity of Thyroid is sufficient to show decided action. Iodothyreine clinically was stated to be without action. The best method of administering the iodised proteid compound which is responsible for the effect is to give to an animal its own biological sort of thyroid hypodermically, human thyroid should be given to the human animal.

It has been reported that thyroid feeding has very marked effect upon the synthesis of urea from ammonia in the liver. The action of the thyroid on the heart is yet without proper explanation. The tachycardia has been explained on the grounds of paralysis of the vagus but more recently the thyroid proteid bodies have been thought to directly injure the heart muscle. Goitre has been produced in normal animals by feeding on water from goitrous springs—these animals being found to have hypertrophied hearts. With regard to etiology of goitre, experiments showed that in individuals drinking from a so-called goitrous well gross enlargement of the thyroid was noticeable after a few weeks unless water were boiled. Water-borne contagion will pass through a Berkefeld filter but will not stand either boiling or heating to 80° C. for half an hour. The infection is therefore either an organism or a very labile chemical compound. A large number of patients develop Graves' disease immediately following severe emotional disturbance or nervous shock. These individuals of course carry a gland capable of reacting to this kind of stimulation, but it is certain that in 40% of the cases the stimulation occurred just before symptoms developed. Antithyroid Serum treatment etc. stated to be effectual—out of 1,500 cases treated 15 to 20% were failures, 50% cured.—“*Recent developments in the Physiology and Pathology of the Thyroid Gland.*”—S. P. Beebe. “*New York Medical Journal*” 8/7/11.

**Thyroid Gland, Seasonal Variation.**—It is stated that three times as much Iodine is found from *June to November* as there is from *December to May*. To obtain 0.2% Iodine one must mix the products of the high and low season of the year.—Jl. Biol. Chem., 1913, 517; Y.B.P., 1913, 39.

Our own experiments and those of Martin and others do not accord with this—at any rate on dry gland.

Martin, P.J. ii./12,144, found as average in the dry gland from July to November, 1911, 0.36%, and in fresh gland 0.091%, and from December, 1911 to May, 1912, in dry 0.33%, and in fresh 0.086%. It is, however, more instructive to compare the content in the months of April to October inclusive with the November to March figures on the fresh gland. The former are about double the latter owing to more moisture content in the winter. The Iodine yield from dry gland works out about the same throughout the year, viz., 0.34%.

N. H. Martin, in continuing his investigations, arrived at 0.25% as a fair Iodine Standard on examination of 13,927 lobes.—P.J. ii./13,123.

Glode Guyer made a prolonged investigation from December 12th to June 13th, on the weights of glands and moisture content. He found the ratio of dry to fresh gland as 1 to 3.6. The Iodine content on fat-free dry gland, through the period, supported our suggested standard of 0.2%.—P.J. ii./13, 123.

R. R. Bennett comments further on *Thyroideum Siccum*. He finds the yield to be 25%, in other words, 1 of dry powder=4 of fresh substance. Martin found (1912) the yield to range from 1=2.58 to 1=5.66, i.e., an average of 1 = 3.39, subsequently (1913) the average was 1 = 4.15. Glode Guyer found in January, 1913, 1 = 3.34 and in June, 1913, 1 = 4.52. The question is raised as to how the old factor 1 = 5 arose.—P.J. ii./13, 804. Probably weight of fresh substance was taken on inadequately trimmed glands.—W. H. M.

## PLACENTA.

An extractive termed **Placentine**, prepared by extracting minced fresh normal placenta with Absolute Alcohol, evaporating to dryness and taking up the residue with normal Saline Solution. Injection of this preparation causes a striking rise in blood pressure following a preliminary fall on injection—chiefly due to constriction of peripheral arterioles. General effect on the circulation similar to that by Adrenalin, but differed in three ways.—(1) Less rapid rise of blood pressure. (2) more prolonged rise, (3) less marked cardiac effect. Should prove a valuable agent administered prior to anaesthetisation in serious abdominal operations—the more so in view of the frequent use of the Scopolamine-Morphine-Chloroform method.—L. ii./07, 1158; P.J. ii./07, 737.

This chemical substance developing simultaneously with the growth of the placenta probably provides stimulus for the production of labour, as it stimu-



lates the uterus to contract. It should be possible to produce the substance synthetically.

**Placentine Solution** from sheep, as prepared by the writer, contains 1% of the extractive in Normal Saline.

(In our opinion and for various obvious reasons it would be very much better to use placenta from animals not subject to tuberculosis and venereal diseases).

As cuti-reaction in pregnancy.—B.M.J., i./14,833.

### Hormones.

**Pro-Secretin**, the remarkable body found by Bayliss and Starling in the columnar epithelia of the small intestine, is an instance of internal secretion by a tissue, the main function of which is of a different nature. This substance when acted on by dilute acid yields **Secretin**, which after passing into and circulating with the blood provokes the secretion of the gastric juice and to a less extent that of the liver, it (Pro-secretin) exemplifies the class of hormones, bodies which give the character to internal secretions, and which, on absorption into the blood, influence tissues and organs other than those from which they have been obtained.

Experiment at University College showed that an acid extractive of the intestinal lining of a dog injected into the veins caused, when reaching the pancreas, an immediate increase in the flow of the pancreatic juice.

The testes and ovary, the intestinal epithelium, the pancreas, thyroid, the suprarenals and the pituitary body appear to yield specific hormones of physiological importance. It is held by some that the internal secretion of the ovary is produced by the corpus luteum.

Milk secretion is not the result of nerve excitation but is controlled by a hormone from the pituitary body.—E. A. Schäfer, Med. Press, March 19, 1913.

The most important ductless glands are the thyroid, parathyroid, pituitary and suprarenal. The cells of a gland have the power of forming one, or possibly more, hormones, each of which has the power of exciting a definite form of chemical activity in those cells for which it has a special affinity. The name **inhibitory hormones** (a contradictory one) is given to substances which, instead of activating may control or inhibit chemical action.—G. R. Murray, L. ii./13,201.

Hormones are thought to have the power to correlate and co-ordinate the various body functions (pregnancy, mammary secretions, etc.), but they also destroy toxins and they control one another—this is the “hormone balance.”—Pres., April, 1913. *c.f.* also Vol. I., p. 587.

**Toad Extract.**—Parotid Secretion of the tropical toad (*Bufo Agui*) has been found to contain two substances—one closely allied to Epinephrin, the other with composition  $C_9H_{12}O_2$  apparently belonging to the Digitalis group of poisons—to this latter the name **Bufagin** has been assigned. To its efficacy it is thought the treatment of cardiac dropsy by toadskin in the Middle Ages was possibly due.—A.M.A., May 27/11, p. 1531. See also P. J. ii./11, p. 96.

## STERILISATION.

**Apparatus.**—For the Bacteriological Sterilisation of Pharmaceutical Apparatus — bottles, mortars, measures, pipettes, ampoules, etc. before filling, chemical cleanliness is first necessary. This can be effected by the use of soap and hot water, rinsing afterwards with tap water, then ‘burning off’ with a little Commercial Sulphuric Acid, rinsing again and drying. The apparatus is then to be heated in a hot (dry) air oven at  $150^{\circ}$  C. for three hours or at  $170^{\circ}$  C. for one hour.

The oven should in preference be a jacketed one having air holes in the inner chamber to allow of circulation of the hot air and it should have a thermometer inserted at the top. An oven of this kind may be improvised, but two points are to be borne in mind. (1) Soldered joints are useless. (2) A shelf or false bottom perforated or so arranged for air circulation must separate the articles from the bottom plate, whereon the flame plays. If it be desired to prepare a supply of utensils in this manner, it is convenient to wrap in stout filter paper, cotton wool or lint, *before* placing in the oven, this wrapping remaining on until the Apparatus in question is required for use. In place of the hot air oven a steam steriliser or Autoclave (a steriliser by steam under increased pressure) may be used, as described under ‘Liquids,’ but on the whole dry heat is best.

**Ampoules, etc.,** for Alkaloidal Salts Solutions should first be washed with Dilute Hydrochloric Acid to remove superficial alkali, and then with clean water before sterilising.

Ph. Ital., orders glass ampoules and bottles for hypodermic injections to be tested as follows for alkalinity:—Ten to twelve ampoules or five to six bottles are filled with a clear solution of 1% Mercuric Chloride, and sealed. After half an hour in an autoclave at  $112^{\circ}$  C. no brownish turbidity should be perceptible.

**Dry Chemicals.**—The sterilisation of these can best be effected by dry heat,—it should, if possible, be as high as  $150^{\circ}$  C. and be continued for at least half an hour,—subject, of course, to the physical characters of the substance permitting it (decomposition, M.Pt., volatilisation, loss of water of crystallisation, etc.); or the sterilisation may be done in the ‘autoclave’ at  $115$  to  $120^{\circ}$  C. for fifteen minutes, but owing to solubility in the steam many dry substances cannot be so treated—for Liquids, however, the Autoclave has many advantages, *v. infra*.

It is convenient in sterilising a bottle full of dry medicament, for example, Boric Acid Crystals or a Zinc Oxide Dusting Powder, to plug the neck of the bottle with a fairly tight wad of cotton wool (preferably previously sterilised to scorching point in the hot air oven). A supply of this wool should find a place in the Dispensary kept in a glass jar with closely fitting lid. The stopper of the bottle is treated separately,—it may be laid alongside the bottle in the oven at the time of heating (ordinary corks are bacteriologically unsuitable). After heating, the bottle and contents are first allowed to cool down gradually—preferably *in the oven* before stoppering,—this ensures that the stopper will not ‘jam.’

It is a good plan to grease the ground surface of the stopper with a minute layer of Soft Paraffin,—this is done *after sterilising* and just



before inserting into the bottle (which is effected simultaneously with the removal of the wool plug) by passing it 2 or 3 times through the Bunsen flame. The whole procedure is carried out as dexterously as possible to prevent access of air organisms. (Note, that bacteriologists would burn the exuding portion of the cotton wool plug and quickly blow it out, leaving sufficient to catch hold of—simultaneously allowing the flame to play on the neck of the bottle also).

*For sterilisation by dry heat, three hours at 150° C. is adequate or one hour at 170° C. (this latter treatment is sufficient to kill all the usual polluting organisms.)—Muir and Ritchie.—We have modified the time requirement somewhat in respect of Dry Chemicals.*

Tawell advises sterilising powdered boric acid by prolonged heating at 98° C. in a carefully regulated air-oven to give satisfactory results. It is liable to undergo change if much heated above 100° C.

### Liquids:—

*The boiling of a liquid for five minutes is, according to these bacteriologists, sufficient to kill ordinary germs if no spores are present. The boiling of any fluid at 100° C. for 1½ hours will ensure sterilisation in almost any circumstances.*

The sterilisation of Liquids may well be done in flasks or other vessels that will stand the heat. Flasks containing liquids plugged with wool as above may be boiled over a Bunsen flame with intervening wire gauze.

*To ensure the killing of spores it is customary to heat liquids where spore contamination is likely (spores of the Tetanus Bacillus, Anthrax Bacillus, and the ubiquitous B. Subtilis, the Hay organism) in an ordinary steamer on three successive days ( $\frac{1}{4}$  to 1 hour). By this treatment all bacilli present are killed on the first day; spores present may develop and are killed on the second day, and the third day is to ensure absolute sterilisation,—this is a modified ‘Tyndall’s Intermittent Sterilisation.’*

*The Spores of the Hay Bacillus are not killed by boiling for about ten minutes (M. and R.).*

Some flint bottles (even ‘Winchesters’) will stand treating in this manner and are more convenient for subsequent transit than flasks. A stoppered bottle should be used.

The subsequent ‘stoppering’ of a bottle of this kind is conducted as described under ‘Dry Chemicals.’ Smearing with Soft Paraffin is essential to prevent subsequent sticking. Working on these lines it is quite easy to bottle off liquids (e.g., Broth used in bacteriological work) prone to rapid bacterial decomposition in such a way as to keep good for years,—indeed indefinitely. Rubber corks are also applicable,—these must be boiled before use.

It is an advantage to heat Solutions in a suitable Steam Steriliser for under pressure practically no evaporation takes place from the Solution, as it is surrounded by an atmosphere saturated with water vapour (quite apart from this, steam sterilisation in general is more efficacious than dry heat). The temperature employed in an autoclave is usually 115 or 120° C. To boil at 115° C. water requires a pressure of about 23 lbs. to the square inch (i.e., 8 lbs. + the 15 lbs. of ordinary atmosphere pressure). To boil at 120° C. a pressure of

about 30 lbs. (*i.e.*, 15 lbs. + the usual pressure) is necessary. *These pressures would usually be called 8 lbs. or  $\frac{1}{2}$  atmosphere and 15 lbs. or 1 atmosphere respectively.* In an autoclave of this kind the desired temperature is maintained by adjusting the safety valve so as to blow off at the corresponding pressure.

**Cautions.**—In all cases it is necessary to allow the Autoclave to cool well below 100° C. before opening, otherwise there will be a sudden development of steam when pressure is removed and fluid will be blown out of the vessels under treatment. Some Autoclaves are not fitted with a thermometer,—in this case expel all air contained initially otherwise a mixture of air and steam being present the pressure read off the gauge cannot be accepted as an indication of the temperature. Furthermore care must be taken to ensure the presence of a residuum of water when steam is fully up, otherwise the steam is superheated and the pressure on the gauge again does not indicate the temperature correctly.—M. and R.

*A single exposure of 15 minutes in an Autoclave is sufficient to destroy all bacilli and spores, provided the steam pressure is at least two atmospheres, *i.e.*, temperature 120° C. approximately—or 15 lbs. pressure on the gauge.*

We now come to the question of *low temperature sterilisation* and take the bacteriologists already quoted as our authorities for the view that '*few ordinary organisms in a spore-free condition will survive a temperature of 57° C. if long enough applied.*' Hence **Solutions or preparations which will not stand boiling** can be rendered practically sterile by heating in a water bath on three successive days at about this temperature—60° to 70° C. is commonly used. The object here is to kill off Spores on the same lines as before and such procedure will obviously kill off the non-spore-bearing pathogenic bacteria.

### *Special Remarks.*

## **Hypodermic Injections and other Solutions of Organic Compounds.—**

Suspensions or Emulsions of Chemical Substances decomposed by heat, *e.g.*, Emulsion Iodoformi, may be prepared by *first sterilising the suspending medium, cooling and then preparing the suspension in a sterilised mortar*,—the same remark applies to Hypodermic injections of decomposable substances in '*Vegetable Oils.*' The Ph. Ital. directs that ordinary Hypodermic Solutions are to be sterilised at 160° C. for 30 minutes or by heating in an autoclave.

According to this Pharmacopœia—Solutions of substances which are decomposed by a temperature of more than 100° C.—*viz.*, Cocaine Hydrochloride, Morphine Hydrochloride, Atropine Salts, Quinine, Eserine Sulphate, Strychnine, Adrenalin, Cacodylates, and Stovain—are to be prepared with Sterile Water and the container then placed in a water-bath for fifteen to twenty minutes, so that the level of the boiling water in the bath corresponds to that of the solution in the bottle. Solutions of *substances decomposed at about 100° C.* are exposed to a temperature of 58° to 60° C. for one hour daily on four consecutive days. This applies to Serums, Organo-Therapeutic Preparations, Ergotin, and Glycerophosphates. Oily Suspensions of Calomel, Yellow Oxide of Mercury, Lecithin, and Camphor are to be prepared with sterile materials, then placed in a boiling water-bath for ten minutes or in an air bath at 100° C.

See also **Morphine Injection for use in War**, Vol. I., p. 516.

*Note.*—We do not agree that all the first mentioned are decomposed as stated at a temperature of more than 100° C.—W. H. M.



## Ophthalmic Solutions.—

Remarks under Apparatus and Hypodermic Injections apply here. In dispensing simple Ophthalmic Solutions required for immediate use, *e.g.*, Atropine, Cocaine, etc., Solutions, in Chalk's Dropping Bottles it will be only practicable to thoroughly steam the measure, bottle, rod, etc., and prepare the Solution by dropping the Alkaloidal Salt into the bulk of the required amount of hot water or other diluent—making up to volume on cooling. *Note.*—Cocaine, Atropine and Eserine Salts are *not* decomposed by this procedure. *N.B.*—*A supply of Chalk's Bottles sterilised by steam and wrapped in Filter paper should be kept ready in the Dispensary.*

**Ointments** may be sterilised by shaking melted ingredients in a closed tin until cold.—C.D. ii./ii,719. In the case of Ointments containing ingredients decomposed by heat it will be necessary to sterilise the non-decomposable item (*i.e.*, presumably the basis), and to incorporate in a sterile mortar with the decomposable items. In some cases the latter may be sterilised by shaking with Alcohol and subsequently with Ether if insoluble in these two liquids.

## Plasters.—

To sterilise a plaster mass the ingredients separately may be heated so far as is possible. A germicide is then incorporated with the mass which will not affect the skin when the spread plaster is applied. A mixture of thymol and methyl salicylate has been recommended, 0.4% of the former and 0.6% of the latter substance added to rubber plaster has been found quite satisfactory. The addition of 1% of phenol to the isinglass solution is useful for court plaster. Plaster wound on spools leaves very little of its surface exposed to the air, and is therefore the least liable to infection.—Pinchbeck, P.J. ii./07,122.

**Surgical Instruments.**—In boiling these (knives, forceps, etc.) to sterilise it is customary to employ a solution of Sodium Carbonate—about 1% is adequate. It is claimed that this prevents rust formation, *c.f.* p. 729.—R. R. Bennett and W. G. U. Woolcock on Sterilisation in Pharmacy, *vide* P.J. ii./09,420,491.

## Surgical Dressings:—

For sterilising Surgical Dressings, the Dressings may well be wrapped in Cotton Wool or in cloths or towels. They are sterilised by superheated steam in a steriliser. (For purposes of transmission and to ensure satisfactory keeping properties the Dressings may be packed in tins.) The air is then exhausted at 20 ins. pressure; steam at 260° F. = 126.6° C. is introduced, and is forced through the Dressings for 20 minutes. The Dressings are finally exhausted by reduced pressure (vacuum of 20 ins.) for 20 minutes and on removal rapidly soldered down. 'Dressings Boxes' are also used with holes in the sides which allow of passage of steam through the Dressings—which are closed instantly on removal—soldering is preferable.

Failing access to a steam steriliser the Dressings wrapped as above may be heated in a current of steam for 1½ hours.

The Vacuum producing arrangement in large sterilisers for this class of work ensures the subsequent thorough penetration of steam into the interior of the Dressings and on completion of the sterilising the steam is completely removed by the re-exhaustion. The Apparatus as made by the best Manufacturers is provided with an air filter to contain Cotton wool or other medium, through which the air is drawn into the chamber at the close of the operation.

The heating of Sterilisers of this description is done either from an existing or separate steam boiler, or by gas burners, or oil burners, or by combination supply alternatively, *e.g.*, steam and gas, oil and gas, oil and steam, as occasion requires. In this way, except in the first case, the Steriliser may, if desired, be worked by steam from an absolutely pure source, *e.g.*, Sterilised Distilled Water.

For testing the efficiency of sterilisation the Tubes Témoins, p. 1, are convenient.

## SYNTHETIC NOTES.

### Physiological effect in comparison with Chemical constitution of Drugs.

There are various theories of the action of Poisons on Cells. That of *Ehrlich*, in which he imagines that the poison becomes attached to the tissues by various chains or anchors before the poisoning can take place, is well known. The theory maintains that when these chains or groups become somewhat altered the union takes place with another cell structure, hence causing a different result.

The theory of *Loew* holds that substances which *can act on Aldehyde or Amino-groups* must be poisons to living tissues—they will act by substitution. According to him the greater the reactivity the greater the physiological result, *e.g.*, **Phenylhydrazine** and **Hydroxylamine** are very reactive to Ketone and Aldehyde groups,—hence poisonous both to plants and animals. *Anilin* is less reactive to Aldehydes than Phenylhydrazine and is less poisonous than the latter. If the chemical properties of a poison are *made more labile* by a change in the character of the molecule, then it becomes *more toxic* and *vice versa*, *e.g.*, if the Hydrogen of the NH group in many alkaloids be replaced by an Alkyl group the toxicity is diminished as the substance reacts less readily with Aldehydes. Similarly Piperidine is more toxic than Pyridine, Tetra-hydroquinoline is far more toxic than Quinoline by reason of the fact that the reduced Compounds which contain secondary Nitrogen in place of tertiary have a greater reactivity with protoplasm. Compare also Pyrogallol (Trihydroxybenzene) which is more poisonous than Dihydroxybenzene (Catechol) and Phenol. The toxicity of Phenols is in the light of this theory attributed to their reactivity,—especially with Aldehyde. *Salicylic Acid* (introduction of COOH) is *less reactive* with Aldehydes than Phenol, hence less toxic. **Loew's Theory** only applies to certain bodies reacting with Aldehyde and Amino groups, it does not explain selective action. Every tissue contains labile Aldehyde and Amino groups,—hence should react with a drug.



Reverting to **Ehrlich's Theory**,—in the example of Morphine it is thought that one of the anchors may be one of the OH groups. If these are combined with  $H_2SO_4$  (forming Morphine-Sulphuric Acid) the substance cannot attach itself to nerve tissue, hence Morphine-Sulphuric Acid has no hypnotic effect. The *entrance of an organic radicle*—Methyl, Ethyl, Acetyl causes the *hypnotic power to be reduced* whilst action on the *respiratory centres* (produced by Morphine to a slight extent) is much *increased, e.g.*, in the case of Codeine and Diacetyl Morphine.

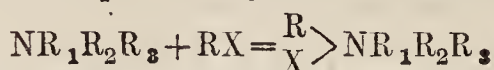
The relationship between Arecoline (the Methyl Ester of Arecaidine) and Arecaidine exemplifies the fact that in cases where the presence of an Acid group prevents the substance from acting physiologically in spite of the presence of an anchoring group, the *conversion of the acid into an Ester* causes the physiological action to appear. The Methyl group in this case does not cause the marked difference,—the effect resides in the Arecaidine which is prevented from showing itself by the Acid group present,—*c.f.*, also Benzoyl-Ecgonine and its Methyl Ester which is Cocaine. Note that analogous effects can be brought about by Ethyl as by the Methyl group. When the Carboxyl group in the molecule is masked we get anæsthetic effect.

With regard to the question of physiological action depending on chemical change of the substances while passing through the organism, a few observations may be offered between some closely related compounds. Wide generalisations cannot be made in these questions,—a case to illustrate this is the decomposition of Xanthine, Theobromine and Caffeine, the first being without action on the heart muscle, the second acting slightly and the third showing more marked toxic action. It was found that the products of metabolism after giving Caffeine and Theobromine contain Xanthine bases poorer in Methyl groups than the substances given,—the Methyl groups had been split off. In man Caffeine is reduced to Theophylline,—this shows that there is a *splitting off of Methyl groups* which groups appear to be responsible for action on the heart, *i.e.*, there is a relationship between physiological action and the changes undergone by the substance in the organism. It is, therefore, often useful in devising new Synthetic Drugs to determine the substances that are formed in the organism when an unsuitable substance is administered. Anilin, for example, is eliminated as Para-amino-phenol,—this led to the introduction of a number of derivatives of this substance of which *Phenacetin* is the best known example. We shall revert to the question of alterations that take place in drugs passing through the system later.

With regard to the Alkaloids in general,—these seem to pass through for the most part *unaltered* and their action is in most cases difficult to explain. It is clear that if a substance is easily acted upon it will react *with all tissues* and hence produce no specific effect. (Hydrocyanic Acid can only be given in small doses for this reason.)

Whilst mentioning Alkaloids we should add the classic discovery

of Crum Brown and Fraser. They showed that various Alkaloids possessing the most diverse physiological actions on combination with Alkyl halides to form quaternary Ammonium derivatives



where  $\text{R}_1\text{R}_2\text{R}_3$  are Organic Radicles of any complexity and  $\text{RX}$  stands for Alkyl halide, Methyl or Ethyl Iodide, etc., yield substances in almost every case possessing the property of paralyzing the motor-nerve endings in the same way as Curare. One can obtain therefore by *Methylation* from all tertiary bases, quaternary Ammonium Compounds which are *poisonous* compared with the original bases. Curare itself contains the tertiary base Curine which is not very poisonous, as well as the far more poisonous Ammonium base Curarine. *Curine on methylation yields Curarine which is 226 times as poisonous as the original substance.*

The fact that the action of Inorganic Salts injected into the blood depends on the *electro-positive* half is analogous with the action of most Esters which generally resembles that of the Alcohol concerned—in both cases the Acids are usually physiologically inert.

Isomorphous Substances in a group have similar action, *e.g.*, Li, Na, Rb, Cs, Ag, Tl, and the physiological intensity usually increases proportionally to the Atomic Weight. Potassium and Ammonium are exceptions. In negative elements, *e.g.*, the halogens, there is no relation between physiological effect and atomic weights.

Ionisation plays an important part in the action of substances, *c.f.*,  $\text{HgCl}_2$  which is ionised in solution and extremely poisonous and  $\text{Hg}(\text{CN})_2$  which is non ionised (though soluble) and far less poisonous, *c.f.*, also  $\text{HgCl}_2$  and  $\text{HgCl}$ .

Meyer and Overton found that practically all narcotics are more soluble in lecithin and cholesterine than in water and they conclude that the narcotic value of a drug depends principally on its solubility in the lipid substances.—J. Grier, B. and C.D. i./13,282.

Schmiedeberg's Rules regarding action of Aliphatic Compounds.

The action of these depends on *volatility and solubility, c.f.*, the lower with the higher members of the series of Paraffins.

(1). Poisonous radicles on substitution by simple Alkyl groups lose in intensity, *e.g.*, Arsenious Oxide,  $\text{O}=\text{As}-\text{O}-\text{As}=\text{O}$  and Cacodyl Oxide  $(\text{CH}_3)_2\text{As}-\text{O}-\text{As}(\text{CH}_3)_2$ .

(2). The effect of the Alkyl groups can on the other hand be lost or lessened by combining with other atoms or groups, *e.g.*, the Mono-Di- and Tri-methylamine behave like Ammonia and have no narcotic action, but the first rule holds here also as these Amines are less toxic than Ammonia.

(3). The action of a body made by uniting two groups by an Oxygen atom depends on the two components each acting separately. Where the two groups are similar or equivalent alkyl groups, *e.g.*, in the Simple and Compound Ethers then the action of the whole is simple and the resulting body resembles in action the



corresponding Alcohol. Analogous are the Esters, the acids of which yield neutral (Sodium) Salts without any specific physiological action. Acetic Ester and its homologues are therefore classed with the Alcohols. If the Acid however has a specific action of its own then this shows itself in the Ester and has a modifying effect on the action of the Alkyl group,—*e.g.*, Amyl Nitrite.

The Hydrocarbons of the Methane series are less active than the *Ethylene, Acetylene or Benzene Series*. In the Methane Series commencing with the lower members we have the *anaesthetic and narcotic action*—this decreasing with loss of volatility and solubility. In the Ethylene series there is also evidence of narcotic action, *e.g.*, Amylene. The Benzene Hydrocarbons show *paralyzing action on motor nerves* and further action on the *brain and spinal cord*.

**Effects of Alkyl Groups**,—in addition to those provided under Schmiedeberg's rules, P. May mentions a number of others. Methyl groups introduced into Aminonia produces Tri-methylamine which is free from convulsive effects, *c.f.*, also the effect of introducing Methyl groups into the Amino group in Anilin, but if the Hydrogen of the nucleus be replaced by Methyl groups there is an increase in the effects, *c.f.*, also the methylation of Xanthine (*antea*). Replacement of the Hydrogen of an Hydroxyl group often reduces activity, *c.f.*, Catechol  $C_6H_4(OH)_2(1:2)$ , Guaiacol  $C_6H_4OH.OCH_3$ , and Veratrole  $C_6H_4(OCH_3)_2$ . Again *Ortho*-methoxybenzoic Acid  $C_6H_4OCH_3COOH$  and Anisic Acid  $CH_3O.C_6H_4.COOH$  are less active than Salicylic Acid  $C_6H_4OH.COOH$ , but this is not invariably true—Resorcin  $C_6H_4(OH)_2(1:3)$  is far less poisonous than Dimethyl-resorcin  $C_6H_4(OCH_3)_2(1:3)$ .

**Ethyl groupings** have a marked influence in causing action on the *central nervous system*, more so than Methyl groups. Another interesting difference between Ethyl and Methyl groups is seen in the case of *para*-phenetol-carbamide  $C_2H_5O.C_6H_4.NH.CO.NH_2$  (Dulcin) which is intensely sweet and the *Methyl analogue* which is *tasteless*.

Ethyl groupings are seen in the following hypnotics. Ethyl Alcohol, Amylene Hydrate, the Sulphonal group, Urethane, Hedonal, Veronal.

Note also the harsh action of Acetanilide is greatly modified by the introduction of the ethyl group as in phenacetin.

**Effect of Phenyl Group**,—no general rule.

**Effect of Hydroxyl Group**.—In *aliphatic bodies* the Hydroxyl group usually weakens action and it is roughly proportional to the number of OH groupings introduced, *c.f.*, conversion of the narcotic Alcohols into Glycols, Glycerol, Mannitol, etc.

The effect is otherwise however in the case of the *aromatic bodies*—the OH usually *increases* effect,—*c.f.*, the obvious case of Benzol and Phenol also Benzoic and Salicylic Acids. The OH very often performs the function of an anchoring group, *e.g.*, for esterification.

Primary Alcohols as a generalisation are less active than secondary and these again less active than the tertiary.

### Effect of Halogen.—

In aliphatic bodies there is *increase in narcotic power*, but there is also an *increase in depressant action* on the heart and blood vessels. The narcotic power and toxicity of Chlorine compounds is well seen in the case of the Chlorhydrins,—narcotics and vasodilators derived from Glycerin which is inert, Tri-chlorhydrin being most active and the Mono-compound least. Note that in the case of the Trichlor- and Monochloracetic Acid the toxicity is reversed. Halogen introduced in the Benzene nucleus causes little alteration in properties. Organic Iodine Compounds differ from those of Chlorine and Bromine in having greater antiseptic and toxic properties and diminished hypnotic effects.

Although the entrance of halogens increases the narcotic action of a drug, the molecule acts as a whole, neither Chlorine nor Bromine being set free in the tissues. Examples: Chloral Hydrate, Tri-chlorbutyl Alcohol.—J. Grier, B. and C.D. i./13,282.

### Effect of Nitro- and Nitroso- Groups.

Either of these whether replacing Hydrogen in the nucleus or in an Hydroxyl Group causes *increased toxicity*. The Aliphatic Nitrites are vasodilators, *c.f.*, Amyl Nitrite. All the Nitrites act in this way, the secondary and tertiary being stronger than the primary, probably owing to the fact that they are more readily hydrolysed to Alcohol and Nitrite. Nitroglycerin and Erythrol Nitrate,—Esters of Nitric Acid show similar action. In the *Aromatic Series* a Nitro Group entering also usually *increases toxicity*.

The effect of the sulphuric ( $\text{SO}_4$ ) group is non-permeating whilst the acetic radicle is, so also the ammonium radicle; this explains why ammonium acetate is actively diuretic whereas ammonium sulphate is slightly cathartic.—J. Grier, B. and C.D. i./13,281.

**Effect of Basic Nitrogen Groups.**—This can produce in either series important changes to which P. May makes various references. The introduction of *Alkyl groupings* into such bodies reduces toxicity and as before gives *hypnotic effect*, *e.g.*, Carbamic Acid  $\text{NH}_2\text{COOH}$  (poisonous) gives Urethane Ethyl Carbamate—more stable and hypnotic. Hydrazine  $\text{NH}_2\text{—NH}_2$  is far more toxic than  $\text{NH}_3$ , but the Tetra- and Penta- Methylene derivatives are non-toxic.

The entry of the Amino Group into the Benzene nucleus forms the groundwork of a large number of antipyretics and analgesics. Anilin like Ammonia produces cramps, but like Benzene it also causes paralysis of muscles and nerves and if one of the Hydrogen atoms of the  $\text{NH}_2$  group be replaced by Alkyl the cramps disappear and the paralysing action remains. If an Hydrogen atom in the nucleus be replaced by a single atom, *e.g.*, Bromine, the cramp effect is retained, and if it is replaced by an alkyl group the effect is increased, but if a complex group, especially



an acid group, *e.g.*,  $\text{SO}_3\text{H}$ , enters the nucleus, the effect is lost, *e.g.*,

in Amino-Benzene—Sulphonic Acid  $\text{C}_6\text{H}_4$   $\begin{array}{l} \nearrow \text{NH}_2 \\ \searrow \text{SO}_3\text{H} \end{array}$ . As a rule aromatic derivatives of  $\text{NH}_2$ , *lower temperature*.

**Effect of the CN radicle.**—Isocyanides (Isonitriles) cause paralysis of the respiratory centre and the Cyanides (Nitriles) produce coma. Neither, however, are as poisonous as  $\text{HCN}$ . The lower members in the fatty series,  $\text{CH}_3\text{CN}$  and  $\text{C}_2\text{H}_5\text{CN}$  are less poisonous than the higher—Cyanacetic Acid  $\text{CNCH}_2\text{COOH}$  is practically non-toxic. Cyanogen Chloride  $\text{CNCl}$  on the other hand is very toxic as it yields readily  $\text{HCN}$ .

### Effect of Aldehyde Groups.—

Formaldehyde is very reactive chemically and therefore physiologically. It is a strong irritant on the mucous membrane. Acetaldehyde produces excitation, and then anaesthesia. Paraldehyde is stronger in action than the latter. *By entry of OH* into the Aldehyde molecule and by condensation of these bodies to form Aldols, *reactivity is lowered*, as also physiological power,—the sugars are practically inert. The aromatic Aldehydes are of low toxicity.

**Effect of Ketones**—Similar to that of Alcohols,—narcotic. An hypnotic action is seen in the Mixed Ketones, *e.g.*, Acetophenone  $\text{C}_6\text{H}_5\text{—CO—CH}_3$ .

**Effect of Acid Groups.** These cause generally a *decrease in activity* or total suppression, *e.g.*, substances containing an OH group on combining with Sulphuric Acid lose their toxicity—Phenol  $\rightarrow$  Phenyl Sulphuric Acid as Sodium Salt  $\text{C}_6\text{H}_5\text{O.SO}_2\text{ONa}$  is harmless, *c.f.*, also Morphine  $\text{C}_{17}\text{H}_{17}\text{NO(OH)}_2$ ,—Morphine-Sulphuric Acid  $\text{C}_{17}\text{H}_{17}\text{NO(OH).OSO}_2\text{OH}$ —this latter, as already referred to, is practically inert. The Sulphonic Acids of various drugs are in nearly every case of little use, the introduction of Carboxyl ( $\text{COOH}$ ) is almost analogous.  $\text{COOH}$  for example reduces toxicity of Benzol which can be taken in doses of 8 Gm. per day to 12 to 16 Gm. of Benzoic Acid. Methylamine  $\text{NH}_2\text{CH}_3$  is toxic.  $\text{NH}_2\text{CH}_2\text{COOH}$  (Glycine) is harmless. The mere *addition of Acid radicles* without converting the body into an Acid may suffice, *c.f.*,  $\text{NH}_3$  poisonous,  $\text{NH}_2\text{CO—CH}_3$  Acetamide practically harmless. Acetanilide is less poisonous than Anilin.

The addition of Acid radicles to active bases is useful in synthesis of drugs,—especially with regard to acetylation of the  $\text{NH}_2$  group,—to weaken basicity and *retard action*. Acetyl, Lactyl, Benzoyl and Salicyl groupings are used, but the *Acetyl* has advantages over the others.

(J. Grier—P.J. ii./11, 533 remarks practically all *synthetic antipyretic* and *analgesic* drugs contain the *acetyl radicle*. Not only so, but it occurs in such naturally occurring pain-relieving drug-principles as aconitine and colchicine.)

**Unsaturated Links.** Unsaturated substances are usually more toxic than the saturated. Allyl Alcohol  $\text{CH}_2=\text{CH}.\text{CH}.\text{OH}$  is strongly poisonous, but is not narcotic. Propyl Alcohol  $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$  is narcotic, but not really poisonous. This relative toxic action is a general property of unsaturated as compared with the corresponding saturated bodies.

**Molecular Weight, Isomerism, etc.—**

Increase in Molecular Weight in homologous series generally produces *increased toxicity*. Several instances in which stereo isomerides differ are given, *e.g.*, Isopilocarpine and Pilocarpine, Maleic and Fumaric Acids, Atropine and Laevo Hyoscyamine, Dextro and Laevo-Nicotine and the natural Adrenalin which is about 11 to 12 times as active as the Dextro compound. With regard to *ortho*-, *meta*- and *para*- Benzene derivatives, no generalisations can be made. *Para*- compounds are often more poisonous than the *ortho*.

With regard to **changes that take place on passing of an organic drug through the system** already referred to, the following is of interest,—*Salts of Organic Acids are generally decomposed into the free acid and a Chloride of the base*, but *Esters* and similar bodies are in the majority of cases *undecomposed* by the gastric contents. In the small intestine, however, the drug encounters the pancreatic enzyme trypsin and an alkaline medium. Trypsin has marked hydrolizing action on Esters, Anilides and similar bodies,—*here after saponification the components of the drug exert their specific action*.—The generally accepted decomposition of Acetyl-Salicylic Acid in the intestine is here pointed out, to which we have devoted some attention, *vide Vol. I., p. 74, and Vol. II., p. 7, et seq.*

Aliphatic bodies suffer usually complete oxidation to Carbon Dioxide, Water and Urea, Aromatic bodies on the other hand maintain the nucleus, the decomposition being concentrated on the side chains.

From the "Chemistry of Synthetic Drugs," by Percy May, B.Sc. (Longmans Green and Co., 1911). By permission of the author.

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Sir William Whitla on the **Trend of Thought in Pharmacological Research**. It is not the number or value of the atoms in a compound which we have to think of but the plan of structure by which they are built up and linked to each other in the drug. Of the empirical formula  $\text{C}_6\text{H}_{12}\text{O}_6$  there are no less than 66 compounds—all totally different.

Brunton and Cash pointed out that all substances built up on the open chain plan—the types of which are Marsh Gas and Chloroform all paralyse the nerve centres and tend to anæsthetic action whilst the ring series produce convulsions or spasms before paralyzing.

In establishing Ehrlich's chemotherapy—effecting *therapia sterilisans magna*, he was really forestalled by Binz, of Bonn, in 1867. The latter experimenting on the action of various drugs on



the infusorial organisms found that active paramecia were readily destroyed by a 1 in 10,000 solution of Quinine though they withstood enormously stronger solutions of Strychnine and other poisonous vegetable substances. This led to the conclusion (the cause of malaria being unknown at the time) that malaria would be found to be of protozoan nature since malaria was so readily cured by Quinine and, secondly, that in giving 15 grains of the Hydrochloride to an average man a solution of twice the strength in the blood necessary to kill amoebae would be formed, thus fulfilling the *therapia sterilisans magna* idea of Ehrlich.—B.M.J. i./13,1145 *et seq.*

Pharmacological Action in relation to Chemical Constitution.—C. R. Marshall, P.J. i./13,622. We refer to this paper elsewhere, *e.g.*, under Nitroglycerin and Erythrol, *Vol. I.*

### PHYSIOLOGICAL STANDARDISATION.

This method of testing is employed in those instances in which the drug contains no definite crystalline, easily isolated, active principle, *e.g.*, an alkaloid capable of extraction.

It consists in "determination of the change in function induced in living organisms by the administration in the state of minute division of such inorganised substances as do not act merely as foods, for the purpose of identifying and adjusting the strength of drugs; this may be either qualitative or quantitative."

The physiological action of a drug is the affinity it possesses for certain constituents of the protoplasm of the cells of particular organs of the body. Thus Ergot has a specific action on the uterus. Cocaine has affinity for nerve endings, and Strychnine acts similarly on the protoplasm of the spinal cord. Furthermore, as a result of the elective principle, drugs, according to their specific action on the organs, are designated stimulant, depressant, or irritant. The animals used for physiological determination should obviously be of the same species and weight, and should have been grown and kept under similar conditions. It is often useful to divide the small animals (*e.g.*, frogs) into classes according to weight, and use these in 'batches' for experimental investigations. Much comparative work has been done with various heart tonics, *e.g.*, Digitalis and Strophanthus (1) by direct application of a solution to the laid-bare frog's heart, and (2) injection intravenously or subcutaneously into dogs, rabbits, &c.

The quantitative test is based on the fact that the killing power of heart tonics for 'similar' frogs is constant per unit of body weight. Comparisons are made between effects produced by the sample preparation under examination and a standard preparation, *e.g.*, a tincture made from genuine Kombé Strophanthus.

Suprarenal Glands and Adrenalin.—Standardisation of these has been effected against a standard freshly made 1 in 1,000 Adrenalin Solution. Adrenalin produces a transitory rise in blood pressure, and the rise is proportional to the amount of actual Adrenalin injected. For outline of technique *vide* also "Notes on Physiological Testing," by A. C. Crawford, *Am. Jl. Ph.*, July, '08, 321; *ibid.* Mar., 1910, 101; Aug., 1910, 360. See N.S.D., 1906, 1732. See also *Vol. I.* of this work for all the above preparations and the chapter on *Digitalis Folia* this Volume.

## PROPRIETARY MEDICINES.

In the following list we provide the approximate composition of Proprietary Medicines—several are mentioned incidentally in the text (all are indexed in the General Index). The '*British Medical Journal*,' the '*Lancet*,' etc., have from time to time published results of analyses, and reference to their pages is made below in each instance. Considerations of space have usually obliged us to mention only the ingredients which have undoubted therapeutic effect. The reader is referred to the original sources for further details. With regard to the great majority of medicines, it should be noted that there are other ingredients which, though for the most part flavourings or colourings, may in some cases be considered to be medicinal. Our list must not be considered complete, though care has been exercised to state therein what appear to be the chief ingredients. The composition of some Proprietary Medicines may be found to vary from time to time. Again the composition of a proprietary article in one country does not necessarily convey a correct impression of articles sold under the same name in other countries.—B.M.J. i./10,339.

The majority of those to which we give B.M.J. references are described in '**Secret Remedies, what they cost and what they contain**,' and in '**More Secret Remedies**,' issued by the British Medical Association, to which we would refer our readers. In some instances we give these books as our only references.

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More or less effective control over the sale of Proprietary Preparations exists in America, France, Italy, Portugal, Russia, and other countries, and in these countries as well as in Austria, Belgium, Brazil, Holland, Hungary, Norway and Sweden, the practice of medicine and of the treatment of diseases and injuries of the body by unqualified persons is forbidden.

Comparison of conditions of Sale of Patent Medicines in various countries.—L. ii./12,1672.

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**Australian Practice.**—Wording respectively permitted and not allowed in advertisements and descriptions of proprietaries.—C.D. i./13,912; B.C.D. i./13,564.

The Australian law modifies Proprietary Medicine advertisements. 'Fruit Saline' was objected to because there was no fruit in it, but as there were mineral substances the manufacturer might label it 'Earth Saline.'—Parry, C.D. i./13,599.

The opinion is expressed that the QUACKERY PREVENTION ACT, 1908, of **New Zealand** might be imitated—any person commits an offence who publishes any statement intended to promote the sale of any article as a medicine for prevention or cure of any ailment or physical defect which is false in any material particular.—Gadd.—B.M.J. i./11,767. We understand, however, that there is a provision in the Act that action can only be taken by Government permission which distinctly detracts from the utility of the measure.

Desirability of enforcing the labelling of Proprietary Medicines and Foods, with a full statement of contents as required by the Pure Food and Drugs Act in **America**.—'State Regulation of Proprietary Medicines and Foods.'—B.M.J. ii./08,574.

The American Medical Association drew up regulations for controlling trade names of pharmaceutical and chemical preparations and issued same to manufacturers of medicinal products.—Chicago March 15/1912.

Regarding **German** legislature *vide* B.M.J. i./08 960. *c.f.* also '*Lancet*' i./08 1086.—A £500 licence was advocated.

Police regulations of 1912 for the **Berlin District** prohibiting the public advertisement of drugs and proprietary medicines.—B.M.J. ii./13,44.

Campaign against proprietaries in **Austria**. Plan suggested was that they should be advertised only in medical periodicals and that labels and containers bear name of article and name of manufacturer only without reference to disease.—P.J. ii./08 686.

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### Patent Medicines and Revenue.

Net receipts from Medical Stamp Duty for the year ending March 31st, 1913, was £328,319 (£325,420 in England, and £2,899 in Scotland), as against £327,857 for 1911-12. The duty does not extend to Ireland.—L. i./13,1562.



The Inland Revenue Authorities hold that an advertisement in a technical journal which does not go to the public does not constitute an advertisement to the public.—C.D. i./13,928.

Dr. Cox, before the Select Committee on Patent Medicines (1912) made the statement that £2,500,000 had been paid by the public since 1908 on Patent Medicines.—C.D. i./12,923.

"The Government reaps a very rich harvest from secret preparations. They have a Government stamp on them, and the Treasury gets many thousands a year out of them,—wrongly, I think. The Government does not think so, however."—Coroner Dr. F. J. Waldo.—P.J. ii./09,303.

Administration of Adulteration Laws.—Sale of Food and Drugs Acts with regard to Proprietary Medicines,—they affect these articles very little. Legislature to make a fresh start and create a new body.—A. W. J. MacFadden, Chief Inspector of Foods under L.G.B.—P.M.C.E., C.D. i./13,874.

The provision of qualified medical advice for the 14,000,000 who come under the **National Insurance Act** will cause a decrease in the sale of Proprietary Medicines.—C.D. i./12,928.

Dixon on Proprietary Patent and Secret Remedies. See P.R.S.M., Therap. and Pharmacol. Sect., Mar. 1910, p. 82.

In B.M.J. of May 27th, 1911, papers on 'Cancer Credulity and Quackery' (see also Cancer Chapter), 'Bone-setting,' 'Quackery and Female Complaints,' 'Skin Diseases and Cosmetics,' 'Unqualified Practice,' 'Quackery in Rural Districts,' 'Quackery in the Past,' 'Herbalists and Medical Practice,' 'Unqualified Practice in the Eye of the Law,' 'Unqualified Practice through the Post,' 'Quackery in Aural Diseases,' 'Quackery in France,' 'Causes of Quackery,' etc., will be found.

The British Medical Association, the British Pharmaceutical Conference, and other Associations joined issue with the Parliamentary Committee on Food Reform to bring the whole subject before a Royal Commission.—P.J. ii./11,69.

The House of Commons appointed a **Select Committee to Enquire into the conditions prevailing in the United Kingdom regarding sale of Patent and Proprietary Medicines.** The Royal College of Physicians, London, made certain recommendations as to the exact composition of the contents of bottles, etc., being printed thereon, and that manufacturers shall not be allowed to print names of diseases or symptoms on same. c.f. C.D. July 1, 1911. We may point out that in certain countries legislation on these lines has been found inoperable.

The Committee met for the first time May 9th, 1912, and received evidence from the Board of Inland Revenue (per Sir N. Highmore) also on May 16th, 1912.—c.f. B.M.J. (May 18th), i./12,1140; C.D. May 18th, 1912.

Subsequently numerous meetings were held and a large number of persons were examined. We have embodied the evidence where of sufficient interest under the appropriate headings. At the same time we have omitted a large number of the preparations which found a place in the last Edition. Recent careful enquiry has shown us that these were in very little demand in commerce.

It should be understood that the authors have no interest one way or the other in providing the following information. It is solely for the guidance of medical men, analysts and pharmacists, and it is not given with any ulterior motive in view.

The authors do not claim to have completely stated all the pros and cons in the matter and the conflicting statements of the analysts giving evidence in the Proprietary Medicine Committee Enquiry. The volumes of the various scientific journals are available for those requiring the information, but even these do not give a complete report of all the evidence.

With regard to the general body of patent medicines, one of the most vexed questions was that of the **publication of formulæ**. Disclosure, not on the label, but to some State Department (either a new central body or one of the existing offices) will probably represent the desire of a section of the Committee. The publication of formulæ would be of no value to the public, while holding out prospects of incalculable harm to proprietors; and it may be taken for granted that should disclosure be insisted upon as essential it will be to a Government body who would be under the strictest obligation to preserve secrecy in regard to the composition of the articles.—C.D. i./13,943.

Publication of formulæ would be of very little advantage to those whom ostensibly the suggestion is intended to protect. Self-drugging would not be reduced. Censorship of advertisements would be an extremely difficult matter. Supervision of constituents would be impossible.—Umney, P.M.C.E., —P.J. ii./12,582; C.D. ii./12,721.

The **Report of the Committee**, issued Aug., 1914, obtainable from Wyman & Sons, Fetter Lane, E.C., found that the existing law offers no check to gross abuse of the public and **recommended the formation of a Government Department—a Ministry of Public Health when created, or in the meanwhile the Local Government Board, to regulate the advertisement and sale of Patent, Secret and Proprietary Medicines and Appliances.**—P.J. ii./14,346; C.D. ii./14,339; c.f. L. ii./14,653,702.

It is intended this Government report shall act as a "reference" to correct any errors which may have crept in either in the Journals from which our information is taken or through oversight in our abstracting.

The B.M.J. published a request for information as to injury caused by Proprietary Medicines, but most of the replies were too general to be of use in the Patent Medicine Enquiry.—C.D. i./12,929.

In selling **proprietary medicines containing poisons** the retailer takes the entire risk—he may sell a poison quite innocently, but he would be liable. —P.M.C.E., C.D. i./12, Ind. fo. 24.

A patient cannot 'patent' a prescription he receives from a consultant. The patent would not be valid, as the patient would not, for one thing, be the "true and first inventor" of the prescription.—E. J. Parry, —P.M.C.E., C.D. i./13,560.

**Difficulties of Analysis.**—Arnica, Bryonia and Buchu have medicinal effect, but science has not been able to state what the active principles are,—these cannot be discovered with certainty by the analyst. Gentian, Mezereon, Hamamelis, Rhubarb and Senna have medicinal effect—in some cases science does not know why. When mixed together it is almost impossible for an analyst to identify them.—P.M.C.E., C.D., July 6/12, Ind. Fol. 23.

Six minims of Ipecacuanha Wine in a six-ounce bottle of water would not be detected by an analyst unless he were put on the track.—P.M.C.E. C.D., July 6/12, Ind. Fol. 23.

**Medicated Wines.**—Necessity of stating Alcohol strength on the labels, —it is often greater than that in light wines.—Dr. Mary Sturge, P.M.C.E. C.D. i./12, Ind. Fol. 5.

## PROPRIETARY MEDICINES WITH REFERENCES.

\* **Abbey's Salt.**—(Aperient) Tartaric Acid, Sodium Bicarbonate, Magnesium Sulphate and Sugar.—L. ii./03,1493.

\* **Alcola (inebriety).**—Three kinds of Tablets.

Ⓢ **No. 1 Tablets** showed the presence of Strychnine 0.12, Caffeine 4.72, Sugar of Milk 86.9, Talc 4.1 per cent. with Starch, a little Gum or Dextrin and a trace of colouring matter. Each tablet would contain 0.007 grain Strychnine and 0.26 grain Caffeine.

Ⓢ **No. 2 Tablets.**—Strychnine 0.2 (approximately), Boric Acid 4.4, Sugar of Milk 82.8, Talc 3.0 per cent., Starch and colouring matter, also a trace of vegetable debris perhaps from some vegetable extract. Each Tablet would contain about 0.011 grain of Strychnine. Ⓢ If less than 2% strychnine.

Ⓢ **No. 3 Tablets.**—Analysis showed Tartar Emetic 16.7, Calcium Sulphate 61.4, Talc 3.1 per cent. with Starch and colouring matter. A trace of a pungent substance resembling pepper, and a trace of vegetable debris which may have been from some vegetable extract—were also present. Each Tablet would contain 0.48 grain Tartar Emetic.—B.M.J. i./12,143.

\* **Allen's Antifat.**—70 minims liquid extract of Fucus in the ounce.—B.M.J. ii./07,209.

\* **Antexema.**—Soft Paraffin 35.4, Boric Acid 1.5, Gummy Matter 12.4, Water 50.7.—B.M.J. i./08,942.

**Antidipso.**—(Drink cure) Chlorate of Potash and Sugar.—L. ii./03,1493.

**White Powders.**—Potass. Brom. 24.5, Milk Sugar 75.5%. Coloured Powder. —Potass. Brom. 35, Milk Sugar 65%.—B.M.J. i./09,910.

**Anti-fat.**—See Allen's above.



\* **Antineurasthin.**—Tablets would contain approximately Dry Yolk of Egg 3·8, Dry White of Egg 5·4, Dry Separated Milk 57·8, Gum 2·0, Potato Starch 22·7, Moisture 8·3%, Aromatic substances traces.—*B.M.J.* i./09,544; see also *P.J.* i./08,644.

\* **Antipon.**—(Obesity).—Contains 39 grains per ounce of Citric Acid.—*B.M.J.* ii./07,25.

**Anturic Bath Salts.**—Analysis showed the salt to consist of Sodium Carbonate (reckoned as Anhydrous) 96·86%, Water 2·70%, Chloride, Potassium salt, perfume, traces.—*B.M.J.* i./10,393.

**Armbrecht's Coca Wine.**—Alcohol 15·05, Glucose 20·8, Coca Alkaloids, 0·006%, *inter alia*. Wineglassful represents about 14 minims of Liquid Extract of Coca.—*B.M.J.* i./09,1307.

**Atkinson & Barker's Royal Infants' Preservative.**—Analysis showed in 100 by measure,—Potassium Bicarbonate 1·75, Magnesium Carbonate 5·45, Essential Oil about 0·06, Alcohol 7·0 by measure, Sugar 9·9, colouring matter a trace.—*B.M.J.* i./12,683.

\* **Balsam of Aniseed.**—See **Powell's**.

**Baring Gould's Antirheumatic Pearls.**—Gelatin Perles or Capsules containing white powder analysis of which showed Acetyl-Salicylic Acid 85%, Milk Sugar 15%.—*B.M.J.* ii./08,1112.

\* **Beecham's Pills.**—(Aperient) Aloes Ginger and Soap.—*L.* ii./03,1493. Quantities as follows were found:—Aloes 0·5 grain, Powdered Ginger 0·55 grain, Powdered Soap 0·18 grain in a pill.—*B.M.J.* i./09,32.

Formula in *S.R.* is stated to be incorrect,—several important ingredients omitted.—A large proportion of the ingredients come from foreign countries. A little over £100,000 was spent in advertising during 1912.—Sir Joseph Beecham, Evidence before Proprietary Medicine Enquiry.—*P.J.* i./13,102; see also Umney, *C.D.* ii./12,723; *C.D.* i./13,563.

Sir J. Beecham admitted having altered his formula.—*E. F. Harrison, C.D.* i./13,650.

**Beecham's Cough Pills.**—In spite of the statement that these do not contain Opium, results obtained pointed to the formula; Morphine 0·0035 grain, Powdered Squill 0·1 grain, Powdered Aniseed 0·3 grain, Ammoniacum 0·3 grain, Extract of Liquorice 0·4 grain.—*B.M.J.* ii./08,1699. The composition has been altered from time to time. Originally they contained some Morphine, then to comply with the Pharmacy Act this was removed,—now it has been replaced in trivial amount and the pills need not be labelled "Poison."—Sir Joseph Beecham, *P.M.C.E.*, *P.J.* i./13,102.

**Bell's \*Fairy Cure.**—Powders each containing Acetanilide and Phenacetin each 1·16 grains, Caffeine 0·38 grain.—*B.M.J.* ii./06,28.

**Bendle's Meat Port Nutrient, White Cap Brand.**

This preparation contains somatose equivalent to 1·4% Protein which represents 7% of raw meat and is a digestive product available for immediate nutrition. A wineglassful (2 ounces) is stated to contain 3·25 drachms of Alcohol.—*B.M.J.* i./09,796. We regret in our last Edition we omitted to add the reference *B.M.J.* i./09, pp. 867 and 964.

This preparation recently formed the subject of an action in the Courts, *Bendle v. United Kingdom Alliance*, in which Mr. Justice Bray gave judgment for the manufacturers.—"*Times*," July 14th, 1914.

\* **Bengue's Balsam.**—Analysis showed the composition to be:—

Menthol 18, Methyl Salicylate 20, Lanolin Anhydrous 54 and a fat, apparently Lard, 8%.—*B.M.J.* ii./10,986.

\* **Bile Beans, Charles Forde's.**—Average weight 2·3 grains. Examination showed Aloin, powdered Cardamoms, Oil of Peppermint, Wheat Flour and possibly presence of Colocynth.—*B.M.J.* i./11,1326.

\* **Bir'ey's Anticatarrh.**—Analysis showed presence of: Sugar 74, Tartaric Acid 1·15, Phosphoric Acid 0·07, Alcohol trace, Water to 100. No free phosphorus could be detected, but odor suggested a trace.—*B.M.J.* ii./08,1286.

**Blair's Gout Pills.**—Active ingredient is Colchicum.—*L.* ii./03,1493. Quantities found indicated Powdered Colchicum Corm. 2·1 grain, Burnt Alum 0·35 grain in one pill.—*B.M.J.* ii./08,1110. ⊕ According to this Analysis.

**Blanchard's Apioland Steel Pills.**—Freed from coating the pills had an average weight of 1·9 grains. Analysis showed presence of Sulphate of Iron, Soap, Barbadoes Aloes, Powdered Ginger, Cardamom and Cinnamon, also a little Apiol.—*B.M.J.* ii./11,36.

**\*Bovril Wine.**—According to analysis a wineglassful (2 ounces) would contain Alcohol  $3\frac{1}{4}$  drachms, Meat Extract 4·4 grains, Glucose 88·0 grains.—*B.M.J. i./09,795.*

**Bowden's Indian Balm.**—A brownish yellow Ointment. The following resembled it,—Lard 35, Cocoa Nut Oil 35, Tallow 10, Rape Oil 5, Lanolin Anhydrous 4·5, Peru Balsam 1, Eucalyptus Oil 5, Terebene 1·5, Essential Oil of Camphor 1·5, Oil of Lemon 0·5, Solution of Ammonia 1, Annatto q.s.—*B.M.J. ii./II, 853.*

**©Bow's Liniment. Syn. Anodyne Liniment.** Dr. Bow's formula : Hard Soap 4, Opium 8, Ammoniated Camphor Liniment 60, macerate and filter. Dr. Bow's modified formula is Ammoniated Camphor Liniment 6, Belladonna Liniment 1, Soap Liniment 6, Strong Ammonia 1, Tincture of Opium 6, Mix, stand 7 days, and filter. These and other formulæ are given.—*P.J.F., 1907.*

**\*Box's Pills (see also Golden Fire).**—Average weight  $2\frac{1}{2}$  grains. The following formula gave a pill substantially agreeing in character with the pill under examination.—Powdered Capsicum 35, Powdered Gentian 15, Flour 15, Aloes 20, Soap 5, Water to 100 parts.—*B.M.J. ii./10,987.*

**©\*Bromidia.**—(Neuralgia) Potassium Bromide, Chloral, Hyoscyamus, Cannabis Indica, Aniseed Oil, Syrup and Water.—*L. ii./03,1493.*

**©\*Brompton Consumption and Cough Specific.**—The formula is approximately Liquid Extract of Ipecacuanha 0·75, Tincture of Opium 1·3 Treacle 75, Water to 100—*B.M.J. ii./08,506.*

**\*Brown's Bronchial Troches.**—Chemical analysis and microscopical examination showed the presence of Powdered Cubebs (also possibly Extract) about 6%, Extract of Liquorice in small quantity, Gum and Sugar (about 70%).—*B.M.J. ii./II,1543.*

**\*Buer's Mul'la Piles Cure.**—Ointment : Galls and Hamamelis, with Lanolin basis. Powder : Precipitated Sulphur and Magnesium Carbonate.—*L. ii./03,1493.*—Later report.—*B.M.J. ii./08,86.*—Anhydrous Lanolin 66·5, Beeswax 1·5, Water 32·0%. Powder.—Precipitated Sulphur 14·9 grains, Calcined Magnesia (partly carbonated), 23·6 grains.

**\*Bunter's Nervine.**—Creosote, Chloroform, Camphor, Balsam of Tolu and Alcohol.—*L. ii./03,1493.*

**Burgeaud's Wine.**—Alcohol 14·80%, Glucose 18·9%, Alkaloids (Cinchona) 0·01%. A wineglassful represents about 2 minims of Liquid Extract of Cinchona.—*B.M.J. i./09,1308.*

**\*Burgess' Lion Ointment.**—The following is similar—Lead Plaster 13, Beeswax 20, Resin 11, Olive Oil 12, Water 6, Lard to 100.—*B.M.J. ii./07,393.*

**\*Burgess' Lion Pills.**—Average weight  $4\frac{1}{2}$  grains without coating. Examination indicated Ipecacuanha, Rhubarb, a little Jalap, probably Aloes (Socotrine), Oil of Peppermint and Soap.—*B.M.J. i./II,1327.*

**\*Bynin Emulsion of Cod Liver Oil with Hypophosphites.**—Oil 34·6%, Reducing Sugars (as Maltose) 9·0%, Protein 1·2%, Hypophosphite in very small quantity.—*B.M.J. i./10,30.*

**\*Bynol.**—Oil 12·9%, Reducing Sugar (as Maltose) 52·2%, Protein 4·6%, Diastatic Power 22.—*B.M.J. i./10,30.*

**\*Cadum.**—Analysis showed Zinc Oxide 11·3, Flowers of Sulphur 8·0, Boric Acid 3·1, Salicylic Acid 0·8, Oil of Cade 7, Hard Paraffin 10, Soft Paraffin 60%.—*B.M.J. ii./10,1352.*

**\*Californian Syrup of Figs.**—Senna (active constituent), Syrup of Figs and Cinnamon.—*L. ii./03,1493.*

**\*Capsuloids.**—Result of analysis indicated for the contents of the Capsules—Hæmoglobin 1·97 grains, Olive Oil and Oleic Acid of each 0·54 grains, Balsam of Peru and Purified Storax 0·17 grain in one Capsule.—*B.M.J. i./08,833.*

**Cardigan Cancer Cures.**—No authentic and unquestionable malignant growth known yielding to the cure.—*B.M.J. i./II,753.*

**Carnabyn.**—Alcohol 17·2, Total Solids 13·4, Nitrogen 0·26 (equivalent to Protein 1·7), Ash 0·7, Reducing Sugar (as Glucose) 9·2%.—*B.M.J. ii./09,562.*

**Carnrick's Liquid Peptonoids.**—100 parts contained Alcohol 20, Total Solids 18·8, Nitrogen 0·8 (equivalent to Protein 5·0), Ash 0·8, Reducing Sugar calculated as Glucose 7·7, Cane Sugar 2·4.—*B.M.J. ii./09,562.*

(Requires spirit licence, but objection is not raised to its sale in small quantities by chemists when ordered by a medical man), c.f. also Vol. I., p. 602.



**\*Carter's Little Liver Pills.**

*B.M.J. i./11,1326 states—Freed from coating average weight of the pill is  $\frac{1}{2}$  grain, evidence of Aloes (Barbadoes) or a preparation of, Podophyllin, Powdered Liquorice Root and Wheat Starch was obtained.*

**Cassell's (Dr.) Blood Cleansing Tablets.**—Weight about 6 grains each. Analysis showed Phenolphthalein 0.75, Pot. Iodide 1.25, Sugar 81, Talc approx. 11, Calcium Carbonate and Sulphate approx. 2, Water 1, Extractive 3%. The dose of Phenolphthalein in one Tablet is 0.045 grain, and the dose of Potassium Iodide is 0.075 grain.—*B.M.J. ii./10,1352.*

**Cassell's Dusting Powder.**—'Antiseptic Dusting Powder No. 2.' Analysis showed Powdered Talc 60, Boric Acid 20, Maize Starch 17, Slippery Elm Bark 3%.—*B.M.J. ii./10,1352.*

**Cassell's Ointment.**—'Ointment No. 2' showed as closely as possible,—Boric Acid 8, Borax 2, Oil of Eucalyptus 2, Oil of Wintergreen 3, Anhydrous Lanolin 4, Oil (? Olive) 8, Soft Paraffin 63, Powdered Drug (? Krameria root) 7, Water 3%.—*B.M.J. ii./10,1352.*

**\*C.B.Q. Post's Tablets** we understand are exempt from Poisons' Schedule, 1908. Analysis made in 1908 showed that each tablet contained  $1\frac{1}{2}$  grains of Potassium Iodide, a small quantity of Salicylate, a vegetable Extract and Magnesia, also a small quantity of Alkaloid which was not identified.—'Secret Remedies.'

Ⓢ **\*C.B.Q. Liniment No. 1.** (No. 2 not poison).

**\*Celmo No. 1.**—The proportions of the various constituents were determined as accurately as practicable, and indicated the following formula—Acetyl-Salicylic Acid 35.5, Powdered Charcoal about 8.0, Malt Extract, dry 18.0, Magnesium Silicate 14.5, other Mineral Constituents 2.8, Water 12.3, Alkaloid 0.5, Extractive about 8.0%. Oleo-resin of Capsicum a trace, Oil of Juniper, a trace.—*B.M.J. ii./10,986.*

**\*Celmo No. 2.**—An analysis showed these Tablets to contain Pepsin, about 3 grains in each Tablet together with Diastase (probably in the form of Malt Extract) and Socotrine Aloes. No evidence was found of any other ingredient.—*B.M.J. i./12,438.*

**Chameleon Oil.**—A mixture prepared by the following formula agreed in physical and chemical properties with the original, except in regard to some minor characters of the Resins. Essential Oils of Mustard 0.75, Spearmint 0.45, Pimento 1.5, Cassia 1.5, and Camphor 13.0, Oil of Turpentine 15.0, Alcohol (90%) 7.3, Strong Solution of Ammonia 8.0, Resins 1.6, and Water to 100. All in parts by measure.—*B.M.J. ii./10,983.*

Ⓢ **\*Chlorodyne, Dr. J. Collis Browne's.**—(Coughs, etc.) Chloroform, Ether, Morphine, Cannabis Indica, Capsicum, Peppermint and Treacle.—*L. ii./03,1493; ii./06,1390.* Does not now contain Hydrocyanic Acid. Pane found practically 2 grains actual Morphine in 1 ounce.—Pharm. Form.

**Cicfa.**—See "Mother's Advice."

**\*Clarke's Blood Mixture.**—Potassium Iodide 52.5 grains, Spirit of Sal Volatile 10 minims, Spirit of Chloroform 67 minims, Simple Syrup 50 minims, Burnt Sugar q.s., Water to 8 ounces.—*L. ii./03,1493 B.M.J. ii./07,530.* Contains no Sal Volatile but an entirely different preparation of Ammonia.—*E. J. Parry, P.M.C.E., C.D. i./13,562; E. F. Harrison's reply, C.D. i./13,651.*

**\*Cockle's (James) Pills.**—Average weight 4 grains. Analysis indicated presence of Aloes, a little Soap, Powdered Colocynth, Powdered Jalap, and another vegetable tissue which did not agree in character with any drug now in ordinary use and which could not be identified.—*B.M.J. i./11,1327.*

**Colman (The) Method.** (For Catarrhs and Cold in the head).

**The Nebular Tablets.**—Average weight of a Tablet 20 grains. Analysis showed them to consist of Sodium Chloride 28.3, Borax (slightly dehydrated equivalent to crystalline Borax) 28.7, Sodium Bicarbonate 29.5, Sugar 12.3, Talc 3.1%, Oil of Wintergreen a trace. The Atomising Liquid was shown to consist of Liquid Paraffin with small quantities of Menthol and Oil of Cinnamon,—traces of other Essential Oils might be present.

**The Gargle Tablets,** average weight of a Tablet 20 grains, Analysis showed them to contain Borax (equivalent to crystalline Borax) 4.6, Sodium Bicarbonate 87.0, Sugar 4.0, Talc 2.1, powdered vegetable drug (possibly Hydrastis rhizome) 1.5%, Turpentine a trace.

**The Pills.**—Average weight  $\frac{3}{4}$  grain. Contain Aloin and indications presence of Jalap Resin and Podophyllin.—*B.M.J. ii./11,1545.*

**\*Coleman's Wincarnis.**—Wineglassful (2 ounces) would contain Alcohol 3 drachms, 8 minims, Meat Extract 10.5 grains, Glucose 159 grains.

—B.M.J. i./09,795. See also *Manufactures in answer to Dr. Mary Sturge.*  
 —B.M.J. i./13,724.

**\* Congreve's Elixir.**—(Cough Mixture).—L. ii./03,1493.

Analysis of the Elixir showed 28.5% by volume of Alcohol together with resinous material similar to the resins of Benzoin, Storax, Tolu or Balsam of Peru, Sugar about 1%. Alkaloid under 0.001%.—B.M.J. ii./08, 505.

Carton round the bottle states 'no poison whatever' and this we have reason ourselves to believe.

**Cotandin Compound.**—Cascara, Hydrochloric Acid, Water.—L. ii./08: 104.

**\* Coza Powders.**—Average weight  $1\frac{1}{2}$  grains, 90% Sodium Bicarbonate, 5% each Cinnamon and Cummin.—B.M.J. i./09,909.

**\* Crosby's Balsamic Cough Elixir.**—Contains inter alia Invert Sugar 58%, Alcohol 10.6%, Acetic Acid 0.3% see B.M.J. (ref.) Sulphuric Acid corresponding to 44 minims of the official dilute Sulphuric Acid in one ounce.—B.M.J. ii./08,1699.

**Curic Wafers.**—Acetanilide 3.28 grains, Phenacetin 3.28 grains, Caffeine Citrate 1.64 grains each.—B.M.J. ii./06,27.

**\* Cuticura.**—Hard and Soft Paraffins, slightly perfumed with rose and coloured green.—B.M.J. i./08,943.

**\* Cuti ura Resolvent.**—Potassium Iodide, Sugar and Glucose, Extractive, Alcohol and Water.—B.M.J. i./08,944.

**\* 'Daisy' Powders** consist of Acetanilide alone, hence exempt from Medicine Stamp Duty. Each powder contains 5 grains.—B.M.J. ii./06,27; L. ii./06, 1390; C.D. i./13,529.

Dixon stated before the recent Proprietary Medicine Committee that Acetanilide is a dangerous drug, and that "lots of deaths" had been caused by headache powders containing it. J. Lawson representing "Daisy" however, pointed out that this is not supported by the Registrar General's returns for the last ten years, only one death being recorded as caused by headache powders (phenacetin), namely in 1908.

Statements have been made that there have been numerous deaths in America from use of Acetanilide. "Daisy" is not intended for Children.—C.D. i./13, 529; P.J. i./13,472.

NOTE.—**\* "BUTTERCUP"** is a trade mark of "Daisy, Ltd."

Details of the introduction of the Company's "Head Powder"—C.D. i./13, 529. These consist of Phenacetin alone. c.f., p. 158.

**Dalby's Carminative.**—Rhubarb, Magnes. Carb., Glycerin, Sugar, Peppermint Oil, Dill Oil, and a small quantity of Laudanum.—L. ii./03,1493. Proprietors say not a poison.

**\* Damaroids.**—Freed from coating the Tablets had an average weight of 3.9 grains. The figures arrived at were Iron Hypophosphite 14.2, Quinine Sulphate 3.4, Extract (probably Damiana) 50, Sugar, Talc 16%.—B.M.J. i./11,27.

**Davis' Famous Female Pills.**—Inter alia, Powdered Savin  $1\frac{1}{2}$  grain in each with Sulphate of Iron.—B.M.J. ii./07,1654. Proprietors say not a poison. A mixture made by them contains Gossypium.—ibid.

**\* "D D.D."** (For eczema). Analysis showed,—Salicylic Acid 0.75, Phenol 1.18, Methyl Salicylate (Oil of Wintergreen) 1.00, Glycerin 9.28, Alcohol 65.10. by measure, Water to 100 parts by measure.—B.M.J. ii./10,1350.

**\* De Roos' (Dr.) Compound Renal Pills.**—Freed from coating average weight of pills was 4.5 grains.—Contained Soap 34.2, Sodium Carbonate 19.7, a Resin (uncertain, probably Ammoniacum) 3.3, and a small quantity of vegetable tissue with moisture and extractive. Vegetable tissue could not be identified.—B.M.J. ii./11,78.

**Dearborn, Ltd's. Preparations.**—'Stalax' and 'Alakite of Orange' before the P.M.C.E.—P.J. i./13,770; C.D. i./13,831; B.C.D. i./13,506.

**Dixon's Pills.**—(Aperient, Liver) Taraxacum, Podophyllin, Jalap and Soap.—L. ii./03,1493.

**\* Doan's (Back-ache Kidney Pills).**—1. White-coated aperient Dinner Pills—Podophyllin, Aloin, Rhubarb and Peppermint 2. Brown-coated (Back-ache) Pills—Oil of Juniper and a resinous constituent (? Benzoin). L. ii./03, 1493. B.M.J. ii./06,1646 gives as similar to the Dinner Pills a pill composed of Podophyllin, Aloin, Peppermint Oil, Jalap, Capsicum and Henbane Extract (this formula would of course be ©); and for the Backache Pills, Juniper Oil, Hemlock Pitch, Potassium Nitrate and Fœnugreek—in both instances with excipients in addition.—Parry has also reported on harmlessness of.



**Doan's Dinner Pills.**—*There is at any rate one most important constituent omitted from above analysis.*—Umney, P.M.C.E., C.D. ii./12,721.

**\*Doan's Ointment** (for piles) Calomel 36·3, Zinc Oxide 11·2, Phenol 1·3, Beeswax 2·3, Soft Paraffin 49·2%.—B.M.J. ii./08,87.

**\*Dodd's Kidney Pills.**—A Pill containing Cascarella, Jalap, Soap, Potassium Nitrate, Sodium Bicarbonate, Hard Paraffin, Turmeric and Wheat Flour is stated to be practically identical.—B.M.J. ii./05,1646.

**Dusart's Wine.**—Alcohol 16·85, Glucose 12·8, Iron 0·09, Calcium 0·07. Phosphorus calculated as Phosphoric Acid 0·03%.—B.M.J. i./09,1309.

**\*Dycol.**—A mixture prepared in accordance with the following formula was practically indistinguishable from the original:—Essential Oils of Mustard 20, Nutmeg 20 and Allspice 4, Cottonseed Oil 6, Liquid Paraffin (yellow) 17, and Kerosene 33%—all by volume.—B.M.J. ii./10,984.

**ⓈEade's Gout and Rheumatic Pills.**—The formula was found to be Barbadoes Aloes 10, Colchicum Extract 18, Colchicum Corm. powdered 35, Treacle 27, Gum and Dextrin 10%.—B.M.J. ii./10,982. Must be labelled with word Poison and name and address of seller.

**Eau de Blanc de Perles.**—Contains *inter alia* about 15% Lead Carbonate.—Murrell

**ⓈEau de Fleurs de Lys** contains a trace of Corrosive Sublimate.—Murrell.

**\*Eczoline Ointment.**—Analysis showed Flowers of Sulphur 39, Zinc Oxide 3·7, Glycerin 13·5, Lard 39·8, Water 4%, Oil of Lemon a trace.—B.M.J. ii./10,1351.

**\*Eczoline Tablets.**—Analysis showed Ferrous Sulphate 16·5, Sulphur. (precipitated) 56, Talc 3·4, Starch 7·3, Extractive 16·8. The Extractive appears to be a mixture of Cascara Sagrada and an inert Extract,—the former constituting about 5% of the substance of the Tablets.—B.M.J. ii./10,1351.

**\*Eno's Fruit Salt.**—(Aperient) Sodium Bicarbonate, Tartaric Acid and Citric Acid.—L. ii./03,1493.

**Epocil**—B.M.J. i./10,762.

**Fell Reducing Treatment.**—Tablets would contain, according to analysis, Extract of Bladder Wrack 0·07 grain, Milk Sugar 0·91 grain (each Tablet had average weight 1 grain).—B.M.J. ii./08,1568.

**ⓈFellow's Compound Syrup** (of) Hypophosphites contains poison.—L. ii./06,1390—*vide also* Vol. I., p. 609.

**\*Fenning's Children's Cooling Powders.**—Average weight 3·4 grains. Analysis showed powder to consist of Potassium Chlorate 70, Powdered Liquorice 30%.—B.M.J. ii./08,1022.

**\*Fenning's Lung Healers.**—Average weight of one pill was 0·22 grains, chemical analysis and microscopical examination showed presence of Ipecacuanha only. Alkaloid present amounted to 1·8%.—B.M.J. ii./11,1543.

**\*Figuroids.**—The large tablets contained by analysis Sodium Bicarbonate 38·9, Tartaric Acid 13·1, Sodium Chloride 3·8, Phenolphthalein 1·2, Formamine (Hexa methylene Tetramine) 2·0 grains. The small Tablets 11·9, 15·9, 7·6, 0·5 grains respectively of the first four.—B.M.J. ii./08,1567; i./09,556.

**Forde's (Chas.) Bile Beans** see Bile Beans.—

**ⓈFreeman's Chlorodyne** 'contains less than 1% Morphine and does not contain Prussic Acid.'—By the Makers.

**\*Fucol** is Sesame Oil containing a small quantity of Iodine. It is said to be made from Seaweed.—B.M.J. i./07,879.

**Gautier's Female Pills.**—Freed from coating the pills had an average weight of 3·8 grains. Analysis showed a small quantity of Aromatic Essential Oils (Pennyroyal, Rue and possibly Tansy) and probably Apiol. Principal constituents were Exsiccated Sulphate of Iron 10% and Soap 11%, Powdered Liquorice 30%, a little Powdered Ginger, and a small quantity of apparently Socotrine Aloes.—B.M.J. ii./11,35.

**ⓈGelineau's Dragées** for Epilepsy are stated to contain Potassium Bromide, 1 in 1,000 Antimony Arsenate and 1 in 2,000 Picrotoxin. (Might be viewed as Ⓢ.)

**\*Genoform.**—Formula of the Tablets is Salicyl-Methylene-Glycol-Ester 95, Starch and moisture 5%.—B.M.J. ii./08,1113.

**Giant Remedy.** The—see Box's Pills and Golden Fire.—

**Glendenning's Beef and Malt Wine.**—Wineglass (2 ounces) contains Alcohol 3·33 drachms, Meat Extract 3·5 grains, Glucose 93 grains.—B.M.J. i./09,796.

**\*Gloria Tonic.**—(*Gout and Rheumatism*) Tablets. The following formula was indicated; Potassium Iodide 1·8, Guaiacum Resin 0·8, Ext. Liquorice 1·0, Resinoid (Phytolaccin?) 0·9 Powdered Liquorice 1·7, Rice Starch 2·0, Talc and Kaolin 2·1 grains. **\*Gloria Pills.**—The following was indicated: Extract of Cascara 0·3, Ext. Soc. Aloes 0·5, Jalap Resin 0·07 grain, Flour and excipient q.s. in one pill.—*B.M.J.* ii./08,1111; see also *L.* ii./03,1493.

**Glykaline.**—(For coughs, colds, catarrhs, etc.) Analysis showed the liquid to contain 35% of Alcohol and 0·15% of solid matter consisting of Potassium Iodide and partly of organic matter. Each dose would contain  $\frac{1}{350}$  grain of Potassium Iodide, with a trace of organic matter which may be derived from some drug.—*B.M.J.* ii./II,1544.

**Goat Lymph Tablets** contain Strychnine Phosphate, Zinc Sulphide, Ext. Muira Puama, Avenine and Cannabin.—*L.* ii./08,104 (Presumably ©.)

We understand these Tablets—one brand at any rate—are only supplied to the medical profession.

**\*Golden Fire.**—The following is the formula given by the analyst:—Oil of Amber 0·16, Oil of Rosemary 0·16, Oil of Eucalyptus 0·32, Oil of Camphor (essential) 1·3, Sodium Chloride 6·4, Glacial Acetic Acid 6·4, Alcohol 1·0 and traces of decoction of Capsicum, Barley and Lobelia.—*B.M.J.* ii./10,987.

**\*Gordon's Vital Sexualine Restorative**, see **Vital Sexualine**.

**\*Gower's Green Pills.**—Analysis showed Soap (about 36%) an alkaline Salicylate (about 37%), Extractive and vegetable tissue—? *Cimicifuga*.—*B.M.J.* ii./08,1112.

**Guy's Tonic.**—Phosphoric Acid, Tinct. Cochineal, Inf. Gentian and Chloroform Water.—*L.* i./03,1493. *B.M.J.* i./11,26 gives the following formula as an exactly similar mixture.—Dilute Hydrochloric Acid 0·59, Dilute Phosphoric Acid 0·52, Alcohol 2·27, Compound infusion of Gentian 40, Chloroform Water 50, Cochineal q.s. Water to 100 parts by measure.

**Hair's (Dr.) Cure for Asthma.**—A fluid containing 5·6% Potassium Iodide, Tar Water and some Wine.—*L.* ii./03,1493; *B.M.J.* i./07,879.

**\*Hall's Wine** originally called **Hall's Coca Wine**—Each bottle contains 1 grain of the extractive principle of Coca leaf and about 17% Alcohol. An overdose is likely to act as its own antidote by causing vomiting—a safeguard against taking excess. Not sufficient Coca present to induce Cocaine habit. For further details see Manufacturer's evidence.—*P.M.C.E.*, *C.D.* ii./12,892; *P.J.* ii./12,751.

**Hammond's Specifics.**—See *Uricura*.

**Hargreaves' Reducing Wafers.**—*Fucus* and *Liquorice*.—*B.M.J.* ii./07,209.

**Harvey's Blood Pills.**—Contain among other ingredients about  $\frac{1}{2}$  grain each Quinine Sulphate, about  $\frac{2}{3}$  grain Potassium Iodide and about  $\frac{1}{2}$  grain *Rhubarb*.—*B.M.J.* ii./07,530.

**Head Powders** prepared by *Daisy Ltd.*, consist of *Phenacetin* alone—8 grains in each.—*J. Lawson*, *C.D.* i./13,530. c.f. also p. 156. *Daisy Powders*.

**Headache Powders** usually contain *Acetanilide*, 3 grains each.

**Healine** (for rupture).—Analysis of Pills gave indefinite results.—c.f. *B.M.J.* ii./08,1198.

**Hochfelder Pitch Plaster.**—*B.M.J.* i./10,761.

**\*Hoffman's Harmless Headache Powders.**—Analysis showed *Acetanilide* 5·02 grains, *Cocoa* 4·02 grains, *Sodium Bicarbonate* 1·01, as one powder.—*Secret Remedies*.

**Hoffmann's (Dr.) Rheumatic Powders:**—

Analysis showed the following composition,—*Acetyl-Salicylic Acid* 66·4 *Phenacetin* 11·4, *Caffeine* 1·3, *Sugar* 20·1, *Moisture* 0·8%.—*B.M.J.* ii./10,982.

**\*Holloway's Ointment.**—Fresh Butter, Beeswax, Yellow Resin, Vinegar of *Cantharides*, Canada Balsam, Expressed Oil of Mace, Balsam of Peru or Liquid Storax.—*Murrell*.

We understand, however, from the makers that this contains nothing of a poisonous nature, and is not ©.

**\*Holloway's Pills.**—*B.M.J.* i./II,1326 states "The Pills had an average weight of 1·4 grains, examination showed the presence of Aloes (*Barbadoes*) or a preparation of Aloes, Powdered Ginger and Soap."

**Holroyd's Gravel Pills.**—Average weight of Pill freed from coating was 4·3 grains. From analysis the following formula was arrived at—Soap 40, Dried Sodium Carbonate 20, Powdered *Rhubarb* 20, Oil of Anise 10, Syrup 10.—*B.M.J.* ii./11,77.



**Hood's Sarsaparilla.**—Dose  $\frac{1}{2}$  to 2 teaspoonfuls. Analysis indicated 19% by volume of Alcohol and  $7\frac{1}{2}$  grains of Potassium Iodide in the ounce, the amount of Sarsaparilla being small.—*B.M.J. ii./07,531.*

**Hood's Vegetable Pills.**—After removal of coating average weight was  $\frac{1}{2}$  grain. Examination showed Aloes (Barbadoes) or a preparation of Aloes,—probably Aloin, Ginger, Capsicum, Colocynth, Soap and probably a little Jalap.—*B.M.J. i./11,1327.*

**Hooper's, Dr. John, Female Pills.**—Analysis showed Iron Sulphate, Aloes, Jalap, Canella, Senna and Oil of Pennyroyal.—*B.M.J. ii./07,1653.*

**\*Horton's Benedict Pills.**—Average weight 4 grains. Analysis showed Sulphate of Iron corresponding to 10% Exsiccated Sulphate, Socotrine Aloes, Powdered Ginger and a vegetable powder probably Gentian.—*B.M.J. ii./11,36.*

**\*Hughes' Blood Pills.**—Contain Aloes, Jalap, &c.—*B.M.J. ii./07,532.*

**Hyomei.**—From analysis and examination it was concluded that Alcohol and Liquid Paraffin formed each about 10% of the whole, Eucalyptus Oil (and possibly other Oils) appears to form the remaining 80%,—a small proportion of a mixture containing Wood Tar and Creosote was also indicated.—*B.M.J. ii./11,1544.*

**\*Imperatine Treatment for Epilepsy,** see Dale's.

**Indian Tincture.**—Capsicum, Cannabis Indica, Ether and Methylated Spirit.—*Murrell.*

**Ⓢ Injectio Brou.**—Zinc Sulphate, Sugar of Lead, Laudanum, Tinct. Catechu and Water.—*Murrell. Pharm. Form. says;—Zinc Sulphate 15 grains, Lead Acetate 30 grains, Catechu Tincture 1 drachm, Tinct. Opii Crocat (q.v.) 1 drachm, Water to 6 ounces, is generally adopted in making imitations.*

**Invigoroids.**—The formula arrived at was:—In one Tablet Ext. Nucis Vom. 0.028 grain, Zinc Phosphide 0.067 grain (calculated from Zinc present). Saccharated Carbonate of Iron 0.50 grain, Asafoetida 0.25 grain with some Sugar of Milk.—*B.M.J. i./11,91. This may be Ⓢ*

**\*Irristum.**—A Syrup of Phosphate of Iron with Quinine.—*B.M.J. ii./07,1658.*

**I.R.S. Compound Golden Tablets.**—Contain Ferrous Sulphate and Sodium Carbonate.—*B.M.J. ii./07,1658.*

**James' Fever Powder.**—Antimonious Oxide 1, Calcium Phosphate 2.

**\*Jefferson Dodd's Corrective.**—Contains Dec. Aloes Conc. with Chloroform Water and Water. Pills are Iron and Aloes.—*B.M.J. ii./07,1654.*

**\*Johnson's (Mrs.) American Soothing Syrup.**—Analysis showed in 100 by measure Sodium Chloride 5.66, Hydrochloric acid (B.P.) 2.33 by measure Reducing Sugars, calculated as Glucose 66.6, extractive coloring matter etc. about 5.0. The reducing Sugars appeared to be present in the form of Honey, representing about 85 parts of this.—*B.M.J. i./12,683.*

The proprietors point out that the preparation does not contain Hydrochloric Acid ("Secret Remedies" and *B.M.J.* state as above), but a third of it is lemon juice. Discussion in the *P.M.C.E.*, C.D. ii./12,23; see also Parry, C.D. i./13,563.

**Juvenia.**—'Liquid No. 1' Solution containing 2% Hydrogen Peroxide,  $\frac{2}{3}$  strength of '10 volume.' 'Liquid No. 2' Paraphenylene Diamine 0.9%, Solution of Ammonia 0.6%, and trace of fixed Alkali.—*B.M.J. i./10,153.*

**\*Kaputine** (for Headache and Neuralgia).—Contains Antifebrin 6.3 grains in each, with Sugar 0.21 grains, and coloured with Ferric Oxide 0.05 grain.—*L. ii./03,1493; B.M.J. ii./06,28.*

**Kargon Compound** contains Fluidextract of Buchu, Potassium Acetate, Methyl Salicylate and Sugar—*L. ii./08,104.*

**\*Karox Compound.**—The contents of several bottles of this preparation were examined and were found to differ very considerably in composition. Magnesium Sulphate varied from 1.45 to 6.87%, Potassium Citrate from 4.76 to 6.55%, Sugars about 8%. The Alcohol in one specimen was 6%, Nitrous Ether was present and a trace of Nitrite, Vegetable Extractive was between 1 and 2% but showed no characters indicative of its source. Microscopical examination of the sediment showed the presence of yeast-like cells and the minute plants known as desmids.—*B.M.J. ii./11,79.*

**Ⓢ \*Kay's Linseed Compound.**

100 parts contained 1.07 parts of Chloroform, and 4.3 parts of Alcohol both by measure, 67 parts of Solids—about 48 parts of the latter sugar, and the remaining 19 parts consisted principally of the mucilage of decoction of linseed. Ipecacuanha alkaloids extracted amounted to 0.007%, and the Morphine to 0.021% *B.M.J. ii./08,1698.*

There is in the S.R. Analysis no mention of Senega which is one of the principal ingredients, while the analysis states that Ipecacuanha is present but there is no mention of it on the label.—Umney, P.M.C.E., C.D. ii./12,891.

\***Kay's Tic Pills.**—Iron Sulphate, Quinine and Soap.—L. ii./03,1493.

©\***Keating's Pectoral Lozenges.**—Corresponded to Morphine 0.007 grain, Ipecacuanha 0.07 grain, Extract of Liquorice 2.1 grain, Sugar 13 grains in one lozenge.—B.M.J. ii./08,1699.

\***Keen's "One Night" Cold Cure.**—Ingredients found were Cinchonidine Sulphate 0.21 grain, Acetanilide 0.32 grain, Calcium Carbonate 0.25 grain, Starch 0.34 grain, Extractive and excipient 0.87 grain (all figures approximately).—B.M.J. ii./08,1286.

\***Kepler Solution of Cod Liver Oil in Malt Extract.**—Analysis showed Oil 17.4%, Reducible Sugar (as Maltose) 42.5, Protein 3.4, Diastatic Power 3.—B.M.J. i./10,30.

\***Ker-nak Pills.**—Average weight without coating  $1\frac{1}{2}$  grain. Examination indicated Aloes, a little Soap, a very little Oleo-resin of Capsicum, and a little vegetable tissue resembling Marshmallow root.—B.M.J. i./11,1327.

\***Kilmer's (Dr.) Ind an Cough Cure.**—Contains inter alia (see ref.) 0.5% Oil of Pumilio Pine No alkaloid.—B.M.J. ii./08,1698

\***Kilmer's (Dr.) Swamp Root.**—The following formula when made up on results of analysis agreed well with the original in degree of bitterness and strength of Wintergreen:—Sugar, 46.5, Alcohol, 10.5, Extract Cascara Sagrada 2, and Oil of Wintergreen 0.5%. The sediment of the original mixture when examined with the microscope showed traces of vegetable tissue in considerable variety.—B.M.J. ii./11,79.

**Kola Wine, Christ's.**—Alcohol 18.85, Glucose 8.6, Alkaloid (with characteristics of Caffeine) 0.03. Each fluid ounce represents  $6\frac{1}{2}$  grains of Kola.—B.M.J. i./09,1307.

\***Koko.**—Borax 1.4, Glycerin 1.7, Formaldehyde Solution (40%) 0.1, Perfume a trace, Alcohol 3, Water to 100 by volume.—B.M.J. i./10,151.

**Lady Webster's Pills.**—Aloes 2 grains, Powdered Mastiche  $\frac{1}{2}$  grain, Red Rose Leaves  $\frac{1}{2}$  grain with Syrup of Wormwood.—Murrell.

**Lamp'ou's Pyretic Saline (Aperient).**—Citric Acid, Potassium and Sodium Bicarbonates.—L. ii./03,1493.

**Lane's (Dr.) Catarrh Cure.**—Analysis showed Phenol 0.4, Sodium Chloride 3.3, Water to 100.—B.M.J. ii./08,1285.

\***Laville's Cough Cure.**—Contains Veratrine.—B.M.J. i./04,1296. Colchicine about 0.08% and Quinine in Alcoholic Solution.—B.M.J. ii./07,877 (latter more likely.—W.H.M.). Either form would make the preparation ©.—It is so labelled.

The following is similar, (Ph. Form 701)—Quinine 4 drachms, Colocynth Extract 2 drachms, Alcohol 90% 4 ounces, Malaga Wine 15 ounces. Mix and filter. Dose,  $\frac{1}{2}$  to 4 drachms in  $\frac{1}{2}$  wineglass of water.

The Pills are (Ph. Form. 744) Extract of Winter Cherry 3 dr., Sodium Silicate 1 dr. Make a mass and divide into 5 grain Pills. Dose, 4 to 10 daily. Guaiacum Resin a constituent with the Silicate and Water Cherry and other ingredients.—Vide Secret Remedies.

\***Lemco Meat Wine.**—A wineglassful (2 ounces) would contain Alcohol 2.75 drachms, Meat Extract 5.2 grains, Glucose 112 grains.—B.M.J. i./09,795.

**Levasco.**—A mixture prepared in accordance with the following formula was practically indistinguishable from the original:—Oleo-resin of Capsicum 3 grains, Camphor 6 grains, Oil of Lavender 3 minims, Oil of Rosemary 4 minims, Soap  $\frac{1}{2}$  grain and Methylated Spirit to 1 ounce.—B.M.J. ii./10,984.

\***Licoricine.**—Does not contain poison.—L. ii./06,1360.

**Liebig's Meat and Malt Wine.**—See Lemco.

**Limosan.**—B.M.J. i./10,762.

\***Liquifruta (A Consumption Cure).**—Analysis showed Oil Peppermint Onion or Garlic Oil and Alkaloids, of each traces, Potassium Bitartrate 0.4, Glucose 34.4, Cane Sugar 2.28, Mucilage, Tannin, Extractive, etc., and water to 100.—B.M.J. ii./09,1419.

**Lockyer's Sulphur Hair Restorer.**—Precipitated Sulphur 1.3%, Lead Acetate 1.6, Lead Sulphate 0.4%, Glycerin 9.6%, Rose Water to 100 by volume.—B.M.J. i./10,151.

**Locock's Pulmonic Wafers.**—Lactucarium, Ipecacuanha and Squills.—Murrell. This form would make the preparation ©.

\***McKenzie's (Dr.) "One Day" Cold Cure.**—Analysis showed the Tablets to have composition Cinchonidine Sulphate 0.83 grain, Acetanilide 0.71



grain, Camphor 0·1 grain, Talc 0·21 grain Water 0·15 grain.—B.M.J. ii./08, 1285.

**Magic Foot Drafts.**—Analysis of the plaster showed the formula to be approximately,—Powdered White Hellebore 40%, Stockholm Tar 60%.—B.M.J. ii./10, 985.

**Maltico.**—Described as a perfect "infant food." Analysis showed Fat 3·9%, Reducing Sugars (as Maltose) 66·5% Protein 16·8%, Ash 4·6%, Water 3·6%.—B.M.J. i./10, 30.

**Mariana Wine.**—Alcohol 36·3, Total Solids 30·3, Ash 0·2, Reducing Sugar (as Glucose) 9·8, Cane Sugar 17·5, Alkaloids 0·025.—B.M.J. ii./09, 562.

★**Marmola.**—Quantitative determination difficult.

Formula arrived at was—Dried Thyroid Gland 1·4 grain, Phenolphthalein 0·4 grain, Sodium Chloride 0·7 grain, Powdered Fucus Vesiculosus 5 grains. Extractive 2·5 grains, Oil of Peppermint trace.—B.M.J. ii./08, 1566 Another analysis, L. ii./08, 104.

**Martin's Apiol and Steel Pills.**—1½ grains of Aloes in each with, *inter alia*, reduced Iron and Apiol each  $\frac{1}{16}$  grain.—B.M.J. ii./07, 1655.

★**Martin's (Dr.) Miracletts.**—Results of analysis indicated Quinine Valerianate 0·4, Zinc Valerianate 0·1, Ferric Oxide 0·3, Menthol 0·03 grain, Kaolin and Talc 2·3 grains.—B.M.J. i./09, 31.

**Martin's Mixture Antidiabeticque.** Apricot Kernel Oil.—L. ii./08, 104.

**Marza Wine** contains Iron, Phosphorus, Coca and Pepsin. Discussion as to quantities.—P.M.C.E., C.D. ii./12, 892.

**Matrozone.**—Analysis of the liquid in a bottle marked "A" showed it to contain 68·9% (by volume) of Alcohol, and water. The total solid matter was too small in amount to be weighed (unless by working on a large amount of the liquid), and might easily be accounted for by tap water having been used to dilute the Alcohol.—No trace of alkaloid was shown by the most delicate test. The liquid in a bottle marked "B" contained 60·3% alcohol by volume, and resembled "A" in other particulars.—B.M.J. ii./11, 37.

**Mattei's Remedy.**—For a reply arising out of the question whether a mixture of sugar and water could be successfully launched as a proprietary medicine. vide P.M.C.E., C.D. ii./12, 24.

**Menstruation Powders.**—Particulars are given of several consisting of Chamomile only.—B.M.J. i./10, 1189.

★**Mer-Syren Powders.**—Indigestion and dyspepsia.

Average weight 25½ grains. Microscopical examination showed the presence of potato starch. No other substance could be detected.—B.M.J. i./11, 1625.

★**Mexican Hair Renewer.**—Precipitated Sulphur 1·4%, Lead Acetate 0·1 (one sample examined contained 0·97%), Glycerin 19·0%, Rose Water to 100 by volume.—B.M.J. i./10, 512.

**Migranol.**—10% Solution of Menthol in Acetic Ether with 4% Spiritus Zondii (q.v. in text) with Camphor and some sweet smelling Ethereal Oils.—B.M.J. i./07, 879.

**Miol.**—Analysis showed it to contain Oil 22·4%, Reducing Sugars as Maltose) 41·3%, Diastatic power 2.—B.M.J. i./10, 30.

★**Monaid Tablets.**—Contain Caulophyllin and Capsicum.—B.M.J. ii./07, 1606.

**Morgan's (Dr.) Radio-Vimettes.** *see* Radio Vimettes.

★**Morison's Pills.**—(For Obesity), One contains Aloes Jalap, Resin, Cream of Tartar, and probably Colocynth; the other some Gamboge as well.—B.M.J. i./07, 832.

**Mothersill's Seasick Remedy.**—Contents of Capsules—a pink and a brown powder on analysis gave the following:—

**Pink Powder.**—Sugar of Milk 33·3, Caffeine 8·2, Stearic Acid 18·0, Chlorbutol 40·1%, colouring matter a trace.

**Brown Powder.**—Powdered Cinnamon 29·4, Caffeine 8·4, Stearic Acid 17·4 Chlorbutol 44·5%. Stearic Acid is probably added as a lubricant to assist in filling the capsules though the amount is large for the purpose.—B.M.J. ii./10, 1928.

★**Mother's Advice.**—Recently Tablenes and formerly 'Cicfa' and before that 'Tablonen.' Contained Pepsin, Diastase and other ingredients.—B.M.J. i./09, 556.

B.M.J. i./11, 1325, gives the following:—Analysis showed presence of Pepsin corresponding to  $\frac{1}{3}$  grain Pepsin B.P., diastase, reducing sugar (apparently Maltose), a bitter extract agreeing in characters with Ext. Cascara Sagrada about

$\frac{1}{100}$  grain, a pungent substance which appeared to be Oleo-resin of Capsicum about  $\frac{1}{100}$  grain, Talc and a little starch probably derived from the coating.

The starch is not converted by Diastase as inferred in S.R.—E. J. Parry, P.M.C.E., C.D. i./13,563.

Mrs. Lydia E. Pinkham's Vegetable Compound *see* Pinkham's  
Mrs. Seymour's Treatment—Obesity *see* Seymour's.

Mrs. Shaffer-Bennyson's Remedy *see* Shaffer-Bennyson's.

Mrs. Stafford-Brookes' Pelloids *see* Stafford Brookes.

Mrs. Terry's Drink Cure *see* Terry's.

★Munyon's Blood Cure and Munyon's Kidney Cure.—Granules, entirely Sugar (quantitative determination showed just 100%).—B.M.J. i./07,213; ii./07,531.

★Munyon's Catarrh Tablets.—Analysis showed Sodium Bicarbonate 1.87 grains, Sodium Chloride 1.81 grains, Borax, partly dehydrated 2.2 grains, Phenol traces, Gum 0.12 grain.—'Secret Remedies.'—B.M.J. ii./08,1286.

★Munyon's Special Catarrh Cure.—Determination showed these pilules to consist of 100% sugar.—B.M.J. ii./08,1286.

★Munyon's Pile Ointment consists of Soft Paraffin with trace of Ichthyol, probably less than 0.2%.—B.M.J. ii./08,87.

Murray's Fluid Magnesia was run by a medical man, physician to the Lord Lieutenant of Ireland, 1859. Advertised in the first number of "Chemist and Druggist."—E. J. Parry, P.M.C.E., C.D. i./13,560; B.M.J. i./13,834.

Nelson-Lloyd Safe Reducing Treatment.—The Tablets contained *inter alia* (see ref.), Bladderwrack Extract and Thyroid gland proteid. Liquid similar.—B.M.J. ii./08,1568, or *vide* Secret Remedies.

★Nervelettes, Coleman's.—Phosphorus 0.005 grain and Quinine Sulphate 0.07 grain with vegetable matter 0.3 grain were determined.—B.M.J. i./09,32.

Ⓒ Neuraline.—Aconite with Chloroform and Rose Water.—Murrell.

Neurovril.—Analysis showed that 100 parts (by measure) contained 18.9 parts (by measure) of Alcohol and gave 19.1 parts of residue on evaporation, of which 18.1 parts consisted of Sugar. No appreciable amount of "serum" or other animal substance was present. If the "active principle" contains as stated on label 75% of Phosphate and 20% of albumen, it follows from the analysis that only a minute trace of it is present in the liquid which is practically a mixture of simple syrup and diluted alcohol.—B.M.J. i./12,26.

Niblett's (Dr.) Vital Renewer.—The formula indicated by results of analysis is in one dose (1 drachm) Potassium Iodide 2.07 grains, Potassium Bromide 15.6 grains, Ammonium Bromide 4.2 grains, Chloroform, Oil of Aniseed, Alcohol and Burnt Sugar, traces.—B.M.J. ii./11,458.

"Normal" Pills.—(For reducing obesity).

Each pill contained approx. Ext. Cascara  $\frac{1}{4}$  grain, Ext. Fucus vesiculosus  $\frac{1}{2}$  grain, Liquorice Powder  $\frac{1}{4}$  grain, Talc and moisture  $\frac{1}{4}$  grain.—B.M.J. i./11,825.

★Norton's Chamomile Pills.—Aloes, Gentian and Chamomile Oil.—Murrell.

★Nurse Lilly's Female Pills.—Freed from coating, average weight was 1.9 grains. Contain Sulphate of Iron, 12%, Socotrine Aloes, Cinchonine Sulphate 3.3%, Powdered Capsicum about 30%, a little Powdered Ginger and Pennyroyal.—B.M.J. ii./11,36.

Orang Blossom Specific for Uterine Diseases.—Principal constituents found to be Alum and Boric Acid, the basis being Soft Paraffin.—B.M.J. ii./09,1419.

★Orphine.—A preparation advertised by the St. George's Association as a cure for the Morphine habit. Analysis showed it to contain Morphine. First dose consisted of 0.374 grain and in course of a month a patient had taken 276 grains to cure him of the Morphine habit.—C.D. i./12,926.

★Osogen.—Determination of the various ingredients gave the following formula: Quinine Glycerophosph. 0.75 parts, Iron Glycerophosphate 2.14 parts, Magnesium Glycerophosphate 0.77 parts, Sodium Glycerophosphate 0.9 parts, Spirit of Chloroform 3.8 parts by measure, Glycerin 73 parts by measure, Water 100 parts by measure.—B.M.J. i./12,27.

Ovaltine.—Described as 'composed of Malt Extract, Fresh Swiss Cow's Milk, Fresh Eggs, and converted Cocoa, and containing active Lecithin.' Analysis showed Fat 12.3%, Reducing Sugars (as Maltose) 60.0%, Nitrogenous substances calculated as Protein 13.4%, Ash 35%, Water 1.5%.—B.M.J. i./10,30.



Glyn Jones' enquiries of Dr. Cox representing the B.M.A., regarding.—P.M.C.E., C.D. i./12,928.

★**Owbridge's Lung Tonic.**—Balsam of Tolu, Oil of Aniseed and Oil of Cloves.—L. ii./03,1493. Does not contain poison.—L. ii./06,1390.

The alkaloids of *Ipecacuanha* were found to the amount of 0.002% If present in the form of Wine of the official strength this represents *Ipecacuanha* Wine 15 m, Chloroform 2 m. in each ounce.—B.M.J. ii./08,1698.

★**Oxien.**—Powdered Sugar, Starch and *Gaultheria* Oil.—L. ii./03,1493.

★**Oxien Medi-Cone Pile Treatment.**—The suppositories weigh on average 19 grains. Analysis showed Lead Acetate 5.6, Croscote about 2 Resinoid substance 3 (showing presence of Tannin), vegetable tissue 1, Hard Paraffin 7 Theobroma Oil 81.4%.—B.M.J. ii./08,87.

**Oxygar.**—B.M.J. i./10,762.

★**Ozerine** (in epilepsy).—Potassium Bromide, Ammonium Iodide with Chloroform Water.—L. ii./03,1493; B.M.J. ii./04,1586, gives approximately Potassium Bromide, 120 grains, Ammonium Carbonate 16 grains per ounce (without Iodide), with Chloroform Water, &c.

**Ozonla.**—Analysis showed the composition of the salt to be: Sodium Carbonate (reckoned as anhydrous) 77.00, Water 22.30, Chloride (reckoned as Sodium Chloride) 0.46%, Potassium Salt a trace.—B.M.J. i./10,393.

★**Paciderma Crème.**—Zinc Oxide, Calcium Carbonate, Calcium Sulphate, Boric Acid and Basis.—B.M.J. i./08,943. q.v. also for Powder and Blood Wafers.

★**Page-Woodcock's Wind Pills.**—Aloes, Caraway Oil and Soap.—L. ii./03,1493; B.M.J. i./11,1326 gives the following, freed from coating the pills had an average weight of 1.6 grains. Evidence of the presence of Aloes (*Barbados*) or a preparation of aloes, a little Ginger, a little Soap, a trace of Capsicum and Oils of Peppermint and Cinnamon, and some indistinguishable vegetable tissue.

**Panopepton.**—100 contained Alcohol 20, Total Solids 26.9, Nitrogen 1.14 (equivalent to Protein 7.2), Ash 1.1, Sugar 7.8.—B.M.J. ii./09,562.

May be dispensed by registered chemists under certain conditions. Vol. I., p. 602.

**Parr's Life Pills.**—Aloes, Rhubarb, Jalap, Gentian, Clove Oil.—Murrell. Pelloids, see *Stafford-Brookes*'.

★**Peps.**—B.M.J. ii./11,1543, summarises results of analysis (q.v. for further details) thus: Sugar about 70%, Extract of Liquorice about 25%, Resinous matter 0.7%, Oil of Peppermint a trace, Oil of Anise a trace, Talc about 4%.

★**Perry-Davis Pain Killer.**—Spirit of Camphor, Tincture of Capsicum, Tincture of Myrrh and Alcohol.—Murrell.

★**Phatolene Tablets.** Analysis showed these ovoid pills of average weight 2.7 grains to consist of Ext. *Fuci Vesiculosi* with about 10% Powdered Liquorice root.—B.M.J. i./11,824.

★**Phelps Brown's Vervain Restorative.**—Decoction of Vervain (2 ozs. to a pint) 4 drachms, Port Wine 1 drachm, Alcohol 2 drachms, Water to 1 ounce. Dose.—2 drachms. Is 25% alcohol.—B.M.J. ii./04,1585. **Phelps Brown's Blood Purifier.** Nothing in particular found beyond 23% Alcohol.—B.M.J. ii./07,531.

**Pink Pills.**—Iron Sulphate, an alkaline carbonate, and Liquorice thickly coated with sugar and coloured with carmine.—L. ii./03,1493. See also *Williams*' Pink Pills.

**Pinkham's (Mrs. Lydia E.) Vegetable Compound.**—Analysis showed it to contain Alcohol 19.3% and Solid Matter 0.6%, traces of Tannin, Ammonia, and Reducing Sugar, also traces of a bitter substance soluble in Ether.—B.M.J. ii./11,33.

**Plant's Cigarettes** (For Asthma).—Leaves of *Stramonium*, *Lobelia*, and Green Tea.—L. ii./03,1493.

**Pond's Arthriticus.**—Analysis of the liquid showed the mixture to have the following composition in one dose approximately: Lithium Citrate 5.0, Potassium Citrate 3.0, Sodium Citrate 0.7, Sodium Salicylate 5.3, Potassium Bromide 5.6, Potassium Bicarbonate 28.0, Glycerin 18.0 grains, in Dilute Chloroform Water. Analysis of the powder to be taken with the mixture showed an average of 14.2 grains of Tartaric Acid per dose.—B.M.J. ii./10,984.

Principal ingredient was formerly Potassium Acetate, but formula was altered by addition of Potassium Bromide and Salicylic Acid. Harrison again analysed and found analysis given in "More Secret Remedies" substantiated.—C.D. i./13,651.

\***Poslam**—Analysis showed approximately Zinc Oxide 12, Flowers of Sulphur 8, Maize Starch 18, Salicylic Acid 1.5, Oil of Cade (?) 1.5, Oil of Birch Tar 8 Anhydrous Lanoline 25.5, Soft Paraffin 25.5%.—*B.M.J.* ii./10,1353.

\***Powell's Balsam of Aniseed**.—Used to contain Morphine but does not now.—*C.D.* i./13,650.

The Manufacturers inform us it contains no ingredient coming within **D** or **Q**.

Parry detected an active ingredient not given in *S.R.*—*C.D.* i./13,563.

**Pritchard's Teething and Fever Powders**.—Dose on lines of *Stedman's v. infra.* Average weight 2.1 grains. Consist of Calomel 47, Antimony Oxide 0.7, Calcium Phosphate 1.4, Milk Sugar 50.9%.—*B.M.J.* ii./08,1022.

**Quina Wine**.—Alcohol 16.9%, Glucose 22.2%, Alkaloid Cinchona (0.05). "Two measures" represent about 10 to 15 minims Liquid Extract of Cinchona.—*B.M.J.* i./09,1308.

**Radol Cancer Cure**.—"An Acid Solution of Quinine."—*P.M.C.E., C.D.* ii./12,605.

**Radium Salve**.—The  $\alpha$ -radioactivity is about  $\frac{1}{160}$  part of that of uranium. The  $\beta$ -radiation is too feeble to be detected by a sensitive electroscope.—*B.M.J.* i./09,1128.

\***Red Cross Pills**.—Freed from coating the pills had an average weight of 2.6 grains. Analysis showed Resin 24.3, apparently Copaiba Resin, a small quantity of Oil of Copaiba, Magnesia 8%, Liquorice and Starch. No other active ingredients were found.—*B.M.J.* ii./11,78.

**Rheumsol Bath Salts**.—Analysis showed the Salt to consist of Sodium Carbonate (reckoned as anhydrous) 87.96%, Water 11.18% chloride, considerable trace, Potassium Salt trace.—*B.M.J.* i./10,393.

\***Rice's Treatment for Rupture**.—An appliance and 'Lymphol.' Careful comparison indicated following for the 'Lymphol.' Tincture of Capsicum made with strong Alcohol 60, Oil of Origanum 6, Oil of Peppermint 1, Oil of Spearmint 0.3, Red Dye, q.s. Rectified Spirit to 100.—*B.M.J.* ii./08,1193.

\***Roche's Embrocation**.—Olive Oil, Oil of Amber, Oil of Cloves, and Oil of Lemons.—*Murrell.*

**Ruspini's Styptic**.—A strong solution of Gallic Acid and Spirit of Roses, with perhaps a little Zinc Sulphate.—*Murrell.*

**Russell's Anti-Corpulent Preparation**.—Citric Acid (about 20 grs. to  $\frac{1}{2}$  oz. a dose), with Water, and a little Iron. The Pink Tablet = Saccharin.—*L.* ii./03,1493; *B.M.J.* ii./07,25.

\***Sacco, also called Lungsalva**, consists of Alcohol, glycerin, and a solid substance identical in its characteristics with *Krameria*.—*B.M.J.* ii./10,563.

\***St. Raphael Tonic Wine**.—"Quinquina."—Alcohol 16.89, Glucose 11.8, Alkaloid (Cinchona) 0.008. A wine-glassful = about  $1\frac{1}{2}$  m. of Liquid Extract of Cinchona.—*B.M.J.* i./09,1308.

\***St. Raphael's Tannin Wine**.—Alcohol 14.65, Glucose 14.0, Tannin (as in ordinary Port Wine), Alkaloid a trace.—*B.M.J.* i./09,1309.

**Sargol**—'A Flesh Producer.' Analysis of the Tablets (average weight 5.3 grains) showed Zinc Phosphide 0.7, Lecithin 1.9, Calcium Hypophosphite 12.9, Sodium and Potassium Hypophosphites 7.7, Albumen (Soluble) 4.2, Insoluble Protein (? Coagulated Albumen) 10.8, Sugar 18%.—*B.M.J.* i./12,846.

\***Savar's Coca Wine**.—Alcohol 23.4%, Glycerin 6.1%, Glucose 2.6, Alkaloid (Coca) 0.07%. Dessertspoonful = about 21 minims of Liquid Extract of Coca.—*B.M.J.* i./09,1307.

**Schaefer's (Dr. J.) physiological nutrient (nerve) salts for neurasthenia** consists of glycerophosphate of Calcium 40 parts, Glycerophosphate of Sodium 30 parts and 20 parts of Sodium chloride with a trace of iron.—*Deut. Med. Woch.*, Sept. 5/10.—*Ex. B.M.J.* ii./10,1900.

**Scott's Pills**.—Average weight 2.4 grs. Examination indicated small quantity of Aloes, Ginger, Rhubarb and Soap.—*B.M.J.* i./11,1326.

**Scott's Emulsion** is stated to have the following composition: Cod-liver Oil 40 litres; Glycerin, 19.875 kilos; Solution of Calcium Hypophosphite 0.8 per cent., 20.450 kilos; Solution of Sodium Hypophosphite 0.4 per cent., 20.150 kilos; Flavouring Essences, 2.970 kilos; Gum, 650 Gm.—*Ph. Notes.*

**Seeger's Hair Dye**.—*W. (Brown)* Pyrogalllic Acid 3.8%, Cupric Chloride (anhydrous) 1.8%, Hydrochloric Acid (*B.P.*) 0.7%, Sulphuric Acid 0.07%.—*B.M.J.* i./10,152.

\***Seigel's (Mother) Syrup**.—

Quantitative determination indicated—

Dilute Hydrochloric Acid (*B.P.*) 10 parts by measure, Tincture of Capsicum 1.7 ditto, Aloes 2 parts, Treacle 60 parts, Water to 100 by measure.—*B.M.J.* i./09,33.



*Correspondence between a doctor and the proprietors.*—*B.M.J.* i./ii,572.

*Manufacturer said it contains 11 different vegetable extracts, not mentioned in above analysis, all possessing definite therapeutic qualities—the relationship of Aloes to the group of Extracts being as 25 to 181.*—*P.M.C.E.*, *P.J.* ii./12,584 *C.D.* ii./12,723.

*Its value in dyspepsia and other affections discussed.*—*C.D.* ii./12,757,787; *Umney's Analysis* *ibid.* 789; see also *B.M.J.* ii./12,1482.

*There are vegetable extracts present not stated in S.R.*—*E. J. Parry*, *P.M.C.E.* *C.D.* i./13,563; *E. F. Harrison's reply* *C.D.* i./13,651.

**Serravallo's Tonic Bark and Iron Wine.**—Alcohol 17·26%, Glucose 6·8, Cane Sugar 12·2, Iron 0·01, Alkaloid (*Cinchona*) 0·05, Liqueur glass represents about 3 minims of Liquid Extract of *Cinchona*.—*B.M.J.* i./09,1308.

**Serum Bantier, 'Anti-gonococcide'** is not a serum, but a Solution of Magnesium-iodo-phenol Sulphonate.—*L.* ii./08,104.

**\*Sequarine.**—The liquid contained Alcohol 35·8%, Oil of Peppermint a trace; on evaporation it left 1·9 per cent. solid residue of which 0·6 was ash,—principally Sodium and Potassium Phosphates. Nitrogen present 0·22 per cent. = to 1·4% of Protein, small portion present as Ammonia, perhaps formed by decomposition of nitrogenous organic matter. Definite constituents could not, of course be isolated.—*B.M.J.* i./ii,27.

**\*Sexualine** see *Vital Sexualine*.

**Seymour (Mrs.) Treatment.**—Obesity. Contained Starch, an extract probably *Fucus vesiculosus*, Boric Acid and possibly a trace of thyroid.—*B.M.J.* i./ii,836.

**Shadeine (Brown).**—Pyrogallie acid 2·1%, Cupric Chloride (anhydrous) 1·3%, Hydrochloric acid (*B.P.*) 0·3%.—*B.M.J.* i./10,152.

**Singleton's Eye Ointment.**—Analysis showed principal ingredient the Red Mercuric Oxide 7·4. Fatty basis contained *inter alia* about 4% beeswax.—*Secret Remedies*.

**\*Standard Malt Extract and Cod Liver Oil.**—Stated to contain 25% Oil. Analysis showed Oil 4·1%, Reducing Sugar (as Maltose) 64%, Protein 5·9, Diastatic Power 74.—*B.M.J.* i./10,30.

**\*Stearn's Headache Cure.**—Powders each contained Acetanilide 3·92 grains, Caffeine 0·98 grain, Milk Sugar 4·9 grains.—*B.M.J.* ii./06,27.

**Stedman's Teething Powders.**—Average weight 2·4 grains. For a child under 3 months the third of a powder; from 3 to 6 months  $\frac{1}{2}$  a powder; when above 6 months a whole powder. The powder consists of Calomel 29% and Sugar of Milk 71%. A trace of alkaloids (not identified).—*B.M.J.* ii./08,1022.

**\*Steedman's Soothing Powders.**—Calomel and Starch.—*L.* ii./03,1493. Average weight 2·8 grains each. Consisted of Calomel 27, Sugar 22, Maize Starch 50·5, Ash 0·5%. Directions similar to Stedman's above.—*B.M.J.* ii./08,1022.

*Australian Customs require statement on the labels "The contents of this package include 27% Calomel." "Calomel has induced sleep." Opium is not present in any form.*—*P.M.C.E.*, *C.D.* i./13,232; *B.M.J.* i./13,350.

**Stevens Consumption Cure.**—According to *B. M. A.* Analysis a preparation of *Krameria*.—*B.M.J.* ii./08,506. See also *ibid.* i./09,672, and *B.M.J.* ii./12,1170,1242,1250,1341; ii./14,211,267.

**\*Sulpholine Lotion.**—Analysis showed Sulphur. precip., 3, Zinc Oxide 2·1, Calcium Sulphate 0·6, Glycerin 9, Strong Rose Water to 100 parts by measure.—*B.M.J.* ii./10,1352.

**\*Swamp-Root, Kilmer's.** see *Kilmer's*.

**Tablones and Tablenes.**—see *Mother's Advice*.

**Tatcho.**—Borax 2·7%, Glycerin 2·5%, Quinine 0·006%, Formaldehyde Solution (40%) 0·38%, colouring and perfume a trace. Alcohol 2·4%, Water to 100, by volume.—*B.M.J.* i./10,151.

**Taylor's Anti-Epileptic Medicine.**—Formula ascertained was Tincture of Iodine  $\frac{1}{4}$  m., Potassium Bromide 13 grains, Ammonium Bromide 4 grains, Water to 1 ounce. Dose,—1 teaspoonful thrice daily.—*Secret Remedies*.

**Terry's (Mrs.) Drink Cure.**—Sugar 98% and Sodium Chloride 2%.—*L.* ii./03,1493.

**\*Therapion No. 3**—Results indicated Camphor 2·5, Glycerin 24, Powdered Liquorice 40, Calcium Glycerophosphate 1·8, Extract of Gentian 5, Extract of Damiana (?) 8, Alkaloid 0·06, Water to 100.—*B.M.J.* i./09,32.

*The Manufacturers inform us 'non-poisonous.'*

**Tissander's (Professor) cure for rheumatism, gout, and sciatica tablets.** Examination showed sulphur salts' (chiefly alkali phosphates) and an emodin

—containing vegetable powder (rhubarb, senna).—*Deut. Med. Woch.* Sept. 13/10 per *B.M.J.* ii./10,1900

**Toris Root Compound.**—Contains Sodium Salicylate, Potassium Nitrate and Sugar.—*L. ii.*/08,104.

\***Townsend's, Old Dr. Jacob, American Sarsaparilla** is similar to the *B.P.* '98 *Liquor Saracæ Comp. Conc.*, but without *Liquorice* and with addition of Sugar.—*B.M.J.* ii./07,530.

\***Towle's Pennyroyal and Steel Pills.**—Contain about 14 grains Dried Iron Sulphate, Capsicum 86 grains, Pennyroyal Oil 3 minims, excipient *s.*,—in 100 pills.—*B.M.J.* ii./07,1653.

\***Tremol Blood Mixture.**—A mixture prepared according to the following formula agrees very well in regard to the vegetable drug and perfectly in other respects. Calcium Chloride 224 grains, Solution of Ferric Chloride 300 minims, Dilute Hydrochloric Acid 200 minims, Concentrated Infusion of Rhubarb (1—7) 100 minims, Peppermint Water 2 ounces, Water to 8 ounces.—*B.M.J.* i./10,1064.

\***Tremol Lotion.**—Analysis showed the liquid to consist of solution of chlorinated soda containing 2·9% of available chlorine.—*B.M.J.* i./10,1064.

\***Tremol Ointment.**—Analysis showed the ointment to contain Prepared Chalk 70·3 parts, Soft Paraffin 29·0 parts, Yellowish brown colouring matter (a coal-tar dye) traces.—*B.M.J.* i./10,1064.

\***Tremol Ointment No. 2.**—The quantities of the different ingredients were determined, and the results agreed with the following formula: Zinc oxide 9·8, Lead Carbonate 3·5, Sodium Benzoate 0·3, Sodium Acetate 0·7, Water 9·6, colouring matter (Pink, evidently a coal-tar dye) traces, Lard to 100 parts.—*B.M.J.* i./10,1064.

**Trench's Remedy for Epilepsy**—Contains about 9 grs. Potassium and 1 grain Ammonium Bromide (concentrated form is 15 grains Potass. Brom. in a powder for a dose.—*B.M.J.* ii./04,1586.

**Trommer's Elixir.**—Stated to contain the active enzymes of Malt, Glycerophosphates, and what is described as the "alkaloidal" extractive of Cod livers.—*L. i.*/10, 653.

**Trommer's Malt Extract and Cod Liver Oil.**—Oil 29·9%. Reducing Sugars (as Maltose) 41·4%, Protein 2·4%, Diastatic Power 35.—*B.M.J.* i./10,30.

\***Trilene Tablets (For Obesity).**—Sugar and a vegetable constituent of unknown nature.—*L. ii.*/03,1493. Minute quantity of Fucus amongst other ingredients, 87% Sugar.—*B.M.J.* ii./07,209.

\***Tuberculozyne (Derk P. Yunkerman Co.) No. I.** Potassium Bromide 3·4, Glycerin 12·0, Cassia Oil 0·1, Tincture of Capsicum 0·17, Cochineal Colouring *q.s.*, Caustic Soda 0·06, Water to 100 gave an exactly similar liquid.

No. II. Glycerin 18, Essential Oil of Almonds 0·1, Burnt Sugar *q.s.*, Water to 100 fluid, gave an exactly similar liquid.—*B.M.J.* ii./08,508.

Bernard Dyer stated the remedy, from analysis of the two samples supplied, consisted chiefly of glycerin flavoured with cinnamon in one sample and almond in the other. One was slightly alkaline and contained phosphates and potassium, the other was slightly acid with minute traces of copper. He understood the solutions were mixed before taking, and said that the amount of copper taken per day would be about  $\frac{1}{100}$  grain. The cost of the treatment was stated to be £2.—*C.D.* ii./08,220.

Tuberculozene is still being sold but its sale is prohibited in Australia.—*P.M.C.E.*, *C.D.* i./12,, *Ind.* fol. 25.

⑥\***Tucker's Asthma Cure.**—According to Dr. Wilcox, Home Office Analyst, in the action against the "*Lancet*" January, 1908, this contains Cocaine 2·28 grains, Atropine 0·87 grain, Sodium Nitrite 15·25 grs. per ounce, 20-30% Glycerin and a trace of Balsam or Benzoin.

A solution of Cocaine Nitrite 1·028, Atropine Nitrite 0·581 in Glycerin 32·16 and Water to 100 is said to produce good results when used in an atomizer. The Nitrites in question are not very stable salts.

Another analysis says Atropine Sulphate 0·15, Sodium Nitrite 0·6, Glycerin 2·0, Water 15·00.—*B.M.J.E.* i./09,43.

Vasey, for the "*Lancet*" found in one sample Cocaine 1·03 grains, Atropine 0·52 grains, Sodium Nitrite 16 grains; in another, Cocaine 1·47 grains, Atropine 0·66 grains, Sodium Nitrite 24·46 grains.—*C.D.* i./08,112; *B.C.D.* i./08 73, *c.f.* also *L. ii.*/03,1493.

The alkaloids in such a mixture may be determined by means of Platinic Chloride and estimating the Nitrogen in the precipitate,—then differentiating



Cocaine from Atropine by precipitation with Potassium Dichromate Solution in strong Hydrochloric Acid.

Another method would be to soak up the fluid in a paste of Lead Oxide and Magnesium Oxide, extract repeatedly with Chloroform, filter, evaporate to dryness, weigh total Alkaloids, then titrate with N/100 Acid (using Phenolphthalein); this gives the amount of Atropine; finally titrate with Methyl Orange, which gives Cocaine.

**Van Vleck's (Dr.) Absorptive Plasma.**—Formula approximately: Powdered galls, 6 parts, Menthol 1 part, Crude Petroleum Jelly to 100 parts. Ditto Food Cones weigh 21 grains. Analysis showed wheat flour 28, Oil of Theobroma 68%, Water 4%, Van Vleck's Pile Pills.—Analysis showed small quantities of Powdered Capsicum, Powdered Liquorice, and Maize Starch, and other ingredients. For further information, vide B.M.J. ii./08, 88,89.

**Van Vleck's Catarrh Balm.**—Analytical results gave formula: Phenol 0·6 Sandal Wood Oil 0·5, Oil of Pumilio Pine 0·7, Eucalyptus Oil 1·2, Soft Paraffin to 100.—B.M.J. ii./08,1283.

\***Vana.**—Alcohol 19·2, Glucose 20·0, Alkaloid (cinchona) 0·23, Calcium 0·01, Phosphorus (combined) as Phosphoric Acid 0·13. A wineglassful=about 3 minims of Cinchona Extract (Liq.).—B.M.J. i./09,1308.

**Varalettes (Bishop's Gout)** showed presence of Lithium Citrate and a small quantity of what appeared to be piperazine with the usual effervescing basis.—'Secret Remedies.'

Ⓢ**Vars, Dr., Kidney Pills (Flexible Capsules)** contain inter alia Peppermint Oil, Juniper Oil, Potass. Nit., Powdered Squill, Henbane and Taraxacum Extract.—B.M.J. ii./06,1646.

**Venc's Lightning Cough Cure.**—Analysis showed inter alia (vide ref.) 0·23% resin, resembling that of Grindelia robusta. It is alkaline, so is the Liquid Extract of Grindelia.—B.M.J. ii./08,1699.

\***Vibrona.**—Alcohol 19·30%, Glucose 6·4, Cane Sugar 5·2, Alkaloid (Cinchona Alkaloids, 0·0297%. — B.M.J. i./09, 1308,1491 and information from the manufacturers.

**Victoria Asthma Drops.**—B.M.J. i./10,762.

**Vigoral.**—Total Solids 50·8, Nitrogen 3·8 (equivalent to Protein 24·0), Ash 16·0%.—B.M.J. ii./09,563.

**Vigoroids** see E. P., XV., Vol. II., p. 96.

**Vilixir.**—(Liquid).—Sulphur precipitated 3·2%, Lead Acetate 1·8%, Glycerin 5·7%, Rosewater to 100 by volume. **Shampoo Powder:** Borax 4·6, Powdered Soap 24·4, Sodium Carbonate (partly exsiccated) 71·0%.—B.M.J. i./10,152.

**Vincent's (Dr.) Anti-Stout Pills.**—Evidence was obtained that they contained Jalap, Colocynth, Cloves, Aloes, or Extract of Aloes, Extract of Fucus Vesiculosus.—B.M.J. i./11,823.

**Vin Regno (Pearson's Liebig's Beef Wine).**—A wineglassful (2 ounces), contains alcohol 2·5 drachms, Meat Extract 2·6 grains, Glucose 65 grains Quinine not identified.—B.M.J. i./09,796.

**Vin Urané Pesqui.**—Analysis showed inter alia in 100 parts by measure, Alcohol 8·75, Glycerin 3·55, total Solids 2·92, Uranium equivalent to Crystalline Nitrate 0·02 (=1½ grain in fluid ounce, or ½ grain in the daily dose).—B.M.J. ii./08,1875.

**Vinsip (Liquor Hæmoglobin Co.).**—Alcohol 8·6, Total Solids 20 2, Nitrogen 2·9 (=Protein 18·2) Ash 1·0 in 100 fluid).—B.M.J. ii./09,562.

\***Virol.**—Analysis showed it to contain Fat 12·3%, Reducing Sugars (as Maltose, 59%), Diastatic power nil.—B.M.J. i./10,29.

\***Vitæ-Ore.**—According to analysis each dose would contain Ferric Oxysulphate 0·47 grain and Magnesium Sulphate Anhydrous 0·15 grain.—B.M.J. i./11 27.

**Wallace's Twelve Specific Remedies.**—No.II. Analysis showed Berberine 0·05, Hydrastine 0·11, Alcohol 32·3 by volume, Extractive 2·7, Ash 0·3. No. III. Analysis showed Caffeine 0·25, Cane Sugar 1·7, Glucose 0·6, Ash 0·52, Alcohol 47·25 by volume, Extractive, 3·13%. A Tincture of pale roasted coffee (1 to 5) appeared to be identical. No. V., Alcohol 30·5 by volume, Ash 0·2, Reducing Sugars 2·9, Extractive 1·7. No. VII., Alcohol 51·05, Ash 0·22, Reducing Sugar 1·0, Fat and Extractive 2·1. A Tincture of Nutmeg (1 to 5) was found to agree in all respects. No. X., Alcohol 26·6, Ash 0·38, Reducing Sugars 0·55, Extractive 1·27. Very like weak Arnica Tincture. No. XI., Caffeine 0·1, Sugars (chiefly cane sugar) 0·7, Ash 0·26, Alcohol 51·05, Extractive 2·1. On same lines as No. III.—B.M.J. i./11,147.

**Wallace's, Gordon, "Treatment."**—Obesity. Freed from coating the Tablets had an average weight of 2.9 grains. Analysis showed them to consist of an extract agreeing with *Fucus Vesiculosus* Extract 2 grains and a vegetable powder, probably *Liquorice Powder*.—B.M.J. i./11,823.

**\*Warner's Safe Cure.**—Potassium Nitrate (about 10 grains to the ounce) and various diuretic herbs.—L. ii./03,1493. A mixture made with Potassium Nitrate 50 grains Alcohol 5 drachms, *Gaultheria* Oil  $\frac{1}{2}$  minim, Liquid Extract of *Taraxacum* 10 drachms, Glycerin 4 drachms, and Water to 8 ounces is almost identical.—B.M.J. i./07,213. An Extract of *Liverwort Leaves* 30, Nitre 15, Glycerin 45, Alcohol 60, with some *Wintergreen Oil*. Pills,—Aloes, Soap, Marsh Mallow, and *Liquorice*.—B.M.J. ii./08,1377.

See also formula presented to German Government authorities by manufacturer.—M.P., Sept. 29./09,347.

**Weidhaas Hygienic Institute.**—See B.M.J. i./09,824.

**\*Welch's Female Pills** (*Kearsley's original Widow Welch's Female Pills*).—Contain Iron Sulphate, Sulphur *Liquorice*, Turmeric with excipient.—B.M.J. ii./07,1654.

**Whelpton's Purifying Pills.**—Weight  $2\frac{1}{2}$  grains. Chemical examination showed Aloes (apparently *Socotrine*), Powdered *Colocynth*, Ginger and *Gentian*. No evidence of Mercury or Calomel.—B.M.J. i./11,1326.

**\*Williams' (Dr) Pink Pills for Pale People.**—Contain Potassium Carbonate, Iron Sulphate and traces of Manganese Oxide and 'Neuræmin' (supposed to be a combination (?) of lecithin, hæmatin and smilacin); the last is from *Sarsaparilla*; also a substance containing Emodin. Some Arsenic is contained in some.—B.M.J. i./07,879.

The quantities found indicated following formula—exsiccated Sulphate of Iron 0.75 grain, Potassium Carbonate 0.66, Magnesia 0.09, Powdered *Liquorice* 1.4. Sugar 0.2, in one pill.—B.M.J. i./09,32. So also B.M.J. i./10,213.—Formula may have been altered.

**Wilson's Patent Ringworm Cure.** See 'Dethblo'.

**Winca-nis,** see Coleman's.

**\*Winslow's, Mrs., Soothing Syrup.**—Previously contained poison, but in November, 1909, was altered—does not come within provisions of Poisons and Pharmacy Act, 1908. c.f. C.D. i./13,650.

Analysis showed it to contain in 100 parts by measure, Potassium Bromide 2.0, Alcohol 4.3 parts by measure, Essential Oil (Anise) about 0.1 part, Sugar 56.5 parts. Emodin was present in small quantity, a Syrup containing 1.2% by measure of the Syrup of *Senna* (Off.), agreed in several respects.—B.M.J. i./12,683.

**Woodcock's Pills,** see Page Woodcock's.

Ⓢ Woodcock's Cough Pills are stated to contain Morphine.

Ⓢ Woodriddle' Gout and Rheumatic Tincture caused death owing to having been taken in overdose, the ingredients include *Colchicum*. The intestines were much inflamed.—W. W. Westcott's Coroner's Case.—P.J. i./13, 17.

**Woodward's Gripe Water.**—Analysis showed in 100 parts by measure, Sodium Bicarbonate 1.08, Essential Oil about 0.03, Alcohol 3.8 parts by measure, Sugar 20.5. The Essential Oil appeared to be chiefly Oil of Caraway, with a little Oil of Dill, and possibly also of Anise.—B.M.J. i./12,683.

"The most important constituent is omitted in the S.R. analysis and those given are inaccurate"—Umney, P.M.C.E., P.J. ii./12,582; C.D. ii./12,721.

Government Analyst, it was stated, failed to find an ingredient and he found certain ingredients that are not contained,—his report on analysis being:—

Alcohol 3.35, Sugar 18.87, Mineral constituents, chiefly sodium bicarbonate 0.92, Essential Oils 0.04, Capsicum Extract a trace, Water 76.82.

The figures are percentages by weight. The mineral constituents in addition to sodium bicarbonate included magnesium, calcium, and potassium, amounting to 0.08. These are probably adventitious, and due partly to the sugar and partly to the water. The quantity of essential oils is too small for chemical discrimination; but the constituents, judging chiefly by odour, consisted mainly of the oils of caraway and dill.

Umney's Evidence, P.M.C.E., C.D. ii./12,890; P.J. ii./12,750. Government Analyst communicated with replied 'No reason whatever to modify terms of report.—C.D. i./13,231, see also E. J. Parry, *ibid.*, p. 563.

Harrison admits trace of pungent aromatic substance.—B.M.J. i./13,947 C.D. i./13,651.

**Yonkerman.**—See *Tuberculozyne*.



\***Zam-Buk.**—*Eucalyptus* Oil 14%, *Pale Resin* (Colophony) 20% *Soft, Paraffin* 55%, *Hard Paraffin* 11%, *Green colouring matter*, a trace.—*B.M.J.* i./08,944.

\***Zip Ointment.**—*Calomel*, *Lead Acetate*, *Lead Oleate*, *Oil* (probably *Olive*) *Creosote*, *Oil of Lemon Grass*, *Paraffin Ointment*.—*B.M.J.* i./08,944

\***Zotos.**—*Capsules* (sea sickness preventive), contained 6.3 grains, pinkish powder consisting of 76.9% *Chlorbutol* (*Syn. Chloretone*), and 23% *Lactose*.—*B.M.J.* ii./09,1419.

\***Zox Powders.**—Average weight  $4\frac{1}{2}$  grains. Consists of *Acetanilide* only.—*B.M.J.* ii./08,1112.

## MINERAL WATERS.

The following information regarding mineral waters has been obtained by applying in most instances direct at the sources.

The arrangement of the paragraphs is as follows:—

The name of the water and locality is given, then follow in order the names of spring or springs, the nature of the water, the chief chemical constituents, the medicinal uses, the season, if any, at the health resort, and an indication as to whether the water is imported in the bottled condition. The accounts of some are, however, condensed. 'Sulphurous' is to convey *Sulphuretted Hydrogen* with (usually *Sodium*) *Sulphates* and *Sulphides*.

See also "Selection of Patients for Spa Treatment."—A recent treatise on the subject.—*N. Wood.*—*L.* ii./09,1276.

Mineral Waters for *Intravenous* and *Intramuscular injections* as Artificial sera. See *Vol. I.* p. 722–726.

Ⓐ We have adhered to the letter of the law viewing mineral waters containing Arsenic as 'Medicinal Preparations of Arsenic,' but obviously we are concerned here *de minimis* in some instances—in others again the amount is very considerable.

**Adelheidsquelle** (BAVARIA).—Saline Tonic, Sodium Chloride and Carbonate, Carbonic Acid. Skin affections, rheumatism, gout, women's diseases. May to Sept.

**Aedipos** (GRECIAN).—Saline thermal. **Aegina** (GRECIAN).—Alkaline. Imported.—*Ph. Notes.*

\***Aesculap** (HUNGARY).—Aperient. Magnesium and Sod. Sulphates, Sodium Chloride and Calcium Sulphate. Occasional and habitual constipation, bowel and liver disorders. Imported. See also Table of Mineral Waters.

**Aix-la-Chapelle** (AACHEN, PRUSSIA).—Saline, Sulphurous. Both drunk and for baths. Sodium Chloride, Sodium Bicarbonate, Sodium and Potassium Sulphates, some Sulphuretted Hydrogen, Carbonic Acid. Rheumatism, gout, stiff joints, skin diseases, syphilis. See also Table of Mineral Waters.

**Aachener Trinksalz.**—Mild aperient, used for gall-stones and liver complaints—blood purifying, also **Aachener Badesalz** strengthening and 'recuperating' in rheumatism, gout, etc., and **Pastillen** of the salts with sugar—for cough and catarrhs, prepared from the above.

**Aix-les-Bains** (SAVOY).—Anti-rheumatic. Sulphur and an organic matter called Baregine, which renders it easy of digestion, oily and suitable for massage. Rheumatism, gout and throat diseases. 1st April to end of October.

**Alet** (AUDE, FRANCE).—Source des Bains and Source Nouvelle.—Alkaline carbonated. Debility, dyspepsia, anæmia. Imported.

**Alexanderbad** (BAVARIA).—Chalybeate. Anæmia, chlorosis, incipient phthisis.

**Alexisbad** (GERMANY). 3 springs: Alexisbrunnen, Schönheitsquelle, Stahlbrunnen or Grotte.—Chalybeate, Iron, Manganese, Potassium Chloride, Free Carbonic Acid. Anæmia, diabetes, nervous diseases and women's diseases.

**Allevard** (ISÈRE, FRANCE).—Sulphurous carbonated. Calc. and Magnesium Bicarbonates, Sodium Chloride Calcium, Sodium and Magnesium

Sulphates, free Sulphuretted Hydrogen, Carbonic Acid and Nitrogen. Chest affections of all kinds, skin diseases, women's diseases, rheumatic complaints, June 1st to September 30th, and imported.

**Alvaneu-Bad** (Near ENGADINE).—Sulphurous. Alpine Climate.

**Andros** (GRECIAN).—Chalybeate. Imported.—Ph. Notes.

\* **Apenta** (near BUDAPESTH).—Aperient. Magnes, Sodium and Calcium Sulphates, Sodium Chloride with small quantities of Lithium and Potassium Sulphates. Habitual constipation, hepatic torpor, congestion, hæmorrhoids, gall stones, gout, uric acid diathesis. See also Table of Waters.

\* **Apollinaris** (NEUENAH, GERMANY).—Acidulated alkali table water Sodium Chloride, Calcium and Magnesium Bicarbonates, with large excess of carbonic acid. Catarrhal affections of the respiratory organs and mucous membrane, acute and chronic laryngitis, bronchitis, dyspepsia, gout and gravel. See also Table of Waters.

**Arabella** (HUNGARY).—Saline aperient. Magnesium, Sodium Sulphates, similar to Apenta. Obesity, gout, rheumatism, liver and kidney disorders. A mild purge.—L. ii./03,322.

⊙ **Baden-Baden** (GERMANY).—Arsenical, Lithiated. Anæmia, chlorosis, gout, dyspepsia, paralysis.

**Baden** (near VIENNA).—Sulphurous. Calcium and Sodium Sulphates; rises warm and contains free Carbonic Acid. Rheumatism, gout, diseases of bones and joints, metallic poisoning, scrofula and syphilis.

**Bagnères-de-Luchon** (HAUTE GARONNE) and **Bagnères-de-Bigorre** (HAUTES PYRÉNÉES, FRANCE) Labassère.—Sulphurous. Skin, lung and rheumatic affections.

**Bagnoles-de-L'Orn** (NORMANDY, FRANCE) Grande Source.—Small quantities of Sodium Chloride, Sodium Sulphate and Silica, also traces of Potassium Iron and Calcium Salts. Used chiefly as baths and douches but is also drunk. Phlebitis, varicocele, women's diseases and rheumatism. May 15th to October 1st, imported.

**Barèges** (HAUTES-PYRÉNÉES, FRANCE).—Sulphurous, warm. Sodium Sulphydrate and Sulphate, Sodium Chloride, Silica. Chronic rheumatism, skin and bone diseases. Imported.

**Barium** (LLANGAMMARCH WELLS, WALES).—Saline. A tumbler full three or four times daily. Sodium, Calcium, Magnesium and Barium Chlorides. Good organically. Only 0.0056 grs. per gallon of Albuminoid Ammonia. Contains no sulphates owing to presence of Barium. Heart affections glandular swellings, skin affections, rheumatism. Bottled, both aerated and still.

**Bath**. The only thermal spring in England, and one of the oldest in Europe. Recent improvements and accommodation. — B.M.J. ii./09, 157. King's Bath Spring.—Calcium Sulphate 102.88 grains, Sodium Sulphate 23.5, Magnesium Chloride 15.8 grains, per gallon, and other Salts in less proportion. Radium has been found in the waters and deposits, also Argon, Helium, Krypton and Xenon.—Pres., May 1911.

King's Well contains 0.1387 mgr. **Radium** per million litres. If the *Niton*\* (emanation) were represented by the weight of Radium capable of forming the Niton present in a million litres of water or gas, the figures for the water of the King's Well, Cross Bath and Hetling Bath are respectively 1.73, 1.19, and 1.7 and for the gas from the King's Well 33.65. The gas from the King's Well contains about four times as much Niton as is contained in the natural gas from Buxton, viz., 7.7 and 8.5 mgr. per million litres.

A patient taking a bath probably absorbs some Niton through the skin and undoubtedly through the lungs. The skin absorption of Niton would be increased by connecting the patient with the negative pole of a battery (at a potential of 100 volts or even more) and placing the other pole in the bath. In a bath containing a cubic metre of Bath water there would be roughly one-thousandth of a milligram of Niton, which apparently is not a dangerous dose. Administration of stronger doses is possible with a spraying-machine, especially if natural gas be used for breaking up the fluid, when the potency

\* Subsequent analysis by Sir W. Ramsay says Niton is present to the extent of  $20 \times 10^{-12}$  Cc. per litre—the largest proportion yet found in a mineral water. The **Dürkheim** springs—the next richest yielding about  $\frac{1}{4}$  this amount. The Radium Content now stated to be about 0.1 mgr. per million litres—which is about the same as Dürkheim water.—P.J. ii./12,25.



would be nearly twenty times that of the water.—Sir Wm. Ramsay. B.M.J. i./12,617; L. i./12,746; P.J. i./12,373. (See also SULIS, *i.e.*, Bath water aerated and bottled).

**Ben Rhydding.** See **Ilkley**.

**Berka** (WEIMAR).—Chalybeate and Sulphurous. In anæmia and rheumatism. 'Moor' and sand baths.

★ **Bethesda** (WISCONSIN, U.S.A.).—Alkaline, Calc. and Magnesium Bicarbonates. Kidney diseases, Bright's disease, diabetes, torpid liver, dyspepsia insomnia. Imported.

**Bilin** (BOHEMIA).—Alkaline acidulated table water, Sodium Carbonate, Sodium Chloride, Sodium Sulphate, Lithium Carbonate, Free Carbonic Acid. Catarrh of the stomach and of the respiratory organs, rheumatism and for Bright's disease. Pastilles are also prepared.

**Birmenstorf** (SWITZERLAND).—Saline aperient. Constipation, jaundice, hæmorrhoids, uric acid. Imported.

★ **Birresborn** (VULKAN, EIFEL, GERMANY).—Alkaline, slightly chalybeate table water, Sodium, Magnesium, and Calcium Bicarbonates, Sodium Chloride, Carbonic Acid. Dietetic.

**Bocklet** (near KISSINGEN, GERMANY).—Chalybeate. Anæmia, nervous and women's diseases.

**Bonifacius** (at SALZSCHLIRF, HESSE-NASSAU).—Saline Lithiated. Gout, gall stones, stimulates intestines and urinary organs. Imported.

**Bonnes** (see EAUX BONNES).

⑩ **Bourboule, La** (PUY DE DOME, FRANCE), Choussy-Perrière Spring.—Arsenated, 1 litre=0.028 Gm. Crystallised Sodium Arsenate (1.9 grs. per gallon), Sodium Chloride and Bicarbonate. *Dose*, a large tumblerful. Debility, anæmia, chest affections, arthritis and diabetes.—B.M.J.E. i./06,60. Imported.

**Brides-les-Bains** (FRANCE).—Alkaline saline. Obesity, uric acid, constipation. Imported.

**Bruckenaue** (GERMANY).—Ferruginous. For women's diseases, anæmia. Imported.

**Brucourt** (CALVADOS, FRANCE). "Star" Spring.—Chalybeate. Tonic in anæmia. Imported.

**Buda-Pesth.** ★ **ST. LUCASBAD** (HUNGARY). (*v.* KRISTALY).—Warm Sulphurous, Potassium, Sodium and Calcium Sulphates Sulphuretted Hydrogen. For bathing, sulphur mud baths, in chronic rheumatism, sciatica, gout, skin affections. Internally, the hot sulphurous springs for intestinal diseases, constipation, hæmorrhoids. Frequented all the year round.

**Buffalo Lithia** (MECKLENBURG CO., VA., U.S.A.).—(No. 2 the chief spring) Alkaline Lithiated table water. Albuminuria, uric acid diathesis, and other affections needing alkaline treatment. June 15 to October 1, and imported.

**Bulgarian Waters.**—43 Springs on the South side of the Balkans.—B.M.J. ii./07,536.

⑩ **Bussang** (VOSGES, FRANCE).—Ferruginous tonic and digestive. Free Carbonic Acid, Sodium, Calcium, Magnesium Bicarbonates with Manganese, Iron and Arsenic. Anæmia, chlorosis, jaundice, gout, rheumatism, diseases of women. Season, 15th June to 15th September. and imported.

**Buxton** (DERBYSHIRE).—Slightly Saline. Sodium Chloride, Magnesium Carbonate, Calcium Carbonate, Free Nitrogen and Carbonic Acid. Stomach, bladder, liver, and kidney disorders, skin affections, gout, rheumatism, sciatica. All the year round and bottled. See also Table of Waters.

The gentlemen's Natural Baths contain 1.1 mgr. per million litres of *Niton*, *i.e.*, about the same as the Cross Baths at Bath.—Sir Wm. Ramsay.—B.M.J. i./12,617; L. i./12,746; P.J. i./12,373.

Valuable in alleviating chronic articular gout and rheumatism—irregular forms of gout are benefitted and acute attacks cut short. The mineral constituents only amount to 27 grains per gallon, chiefly Carbonates of Calcium and Magnesium, Sodium Chloride with traces of Iron and Manganese. The gases contained show a unique richness in Nitrogen. We have yet to learn why radio-active properties minister to gout and rheumatism. So far as is known radio-activity exerts a healthy active influence over metabolism.

★ **Cachat** (see EVIAN, Source Cachat).

★ **Cambrunnen** (TAUNUS, GERMANY).—Alkaline dyspepsia, rheumatic affections, skin diseases.

**Capvern** (HAUTES PYRÉNÉES, FRANCE).—2 springs; Houn-Caoude (drinking) and Bouridé (baths). Alkaline. Catarrh of bladder, gravel, gall stones women's diseases. Season, May to October. Imported.

**Carabana** (SPAIN).—Purgative. Sodium Sulphate. Intestinal and hepatic affections and dyspepsia. Imported.

**\*Carlsbad** (BOHEMIA).—Several similar springs.; that known as **\*SPRUDEL** is the most favoured. Alkaline, Lithiated. Obesity, constipation, stomach, intestinal, liver, kidney and bladder disorders, gout and diabetes. Imported.

**\*Carlsbad Sprudel** salts (powder and crystals) are also supplied. See also Table of Waters.

**Cauterets** (PYRÉNÉES).—Sulphurous. Sulphuretted Hydrogen, Iodine. Skin and lung diseases, glandular swellings. Summer and imported.

**Cerigo** (GRECIAN).—Chalybeate. Imported.—Ph. Notes.

**Challes** (SAVOY).—Sulphurous. Chronic catarrh, skin affections and intestinal diseases. May to October. Imported.

**Charlottenbrunn** (SILESIA).—Chalybeate.

**Chateldon** (PUY DE DOME, FRANCE).—Alkaline Acidulated. Stomach and urinary disorders, anæmia, and as a table water. Imported.

**Chatel Guyon** (AUVERGNE, FRANCE). Source Gubler.—Alkaline. Dyspepsia, jaundice, anæmia, constipation, uric acid. May to October. Imported.

**\*Cheltenham**.—Pittville Waters: No. 1 Cheltenham Alkaline, Sodium Chloride, Sulphate and Bicarbonate; No. 2 less Sodium Chloride more Sulphate; No. 3 more Sodium Sulphate but less than No. 2; No. 4 Cheltenham 'Magnesia' (Magnes. Sulphate 117 grains per gallon) and Sodium Sulphate, No. 5 is No. 4 concentrated. No. 6 is Cheltenham Sodium Sulphate Saline, Sodium Sulphate in predominance. See also Table of Waters.

**Claudia** (SORGENTE DI ANGUILLARA, SABAZIA, near ROME).—Alkaline. Carbonic Acid with small quantities of Alkaline Bicarbonates. Gastric dyspepsia. Imported.

**Condal** (RUBINAT, LÉRIDA, SPAIN).—Aperient, Sodium, Magnesium, Calcium and Potassium Sulphates, Sodium Chloride. As a purgative for habitual constipation, plethora &c. Imported. See also Table of Waters.

**Condillac** (FRANCE).—Alkaline acidulated table water. Imported.

**Contrexéville** (VOSGES, FRANCE). Pavillon Spring.—Alkaline, Anti-rheumatic. Gouty affections, dyspepsia, eczema, catarrh of the bladder and liver. 20th of May to 20th of September, and imported. Contrexéville Source Mignon is also supplied. See also Table of Waters.

**Dax** (called locally La Néhe). Thermal—has temperature 61° C. Owing to evolution of Nitrogen appears to be boiling. Contains Sulphates and Chlorides of Calcium and Sodium. The mud contains a large proportion of living algæ—the *Oscillaria calida*. Is distinctly radio-active. In rheumatism. —B. & C.D. i./o6,67.

**Desaignes** (Eau de César) (ARDÈCHE, FRANCE).—Alkaline, Acidulated. Table water. Imported.

**Dolecoed**. See **Llanwrtyd**.

**\*D'Orezza** (CORSICA). Chalybeate table water. Anæmia, dyspepsia; useful after prolonged illness, or for weakness. 1st July to 1st September. Imported.

**Driburg** (WESTPHALIA).—Chalybeate, Tonic, Aperient. Sodium Sulphate Magnesium Sulphate, Bicarbonate of Calcium, and Magnesium, some Iron and Manganese, Carbonic Acid. Stone in the kidney and kidney diseases generally, neurasthenia, nervous diseases, women's diseases, anæmia.

**Droitwich**. See **\*Wychia**.

**Dürkheim**. See also **Bath**.

The Max Spring found to contain 17.2 to 17.3 mgr.  $\text{As}_2\text{O}_3$  per litre—the largest content of any spring excepting Roncegno *q.v.* Contains also Rubidium and Caesium.—P.J. i./12,689.

**Eaux Bonnes** (BASSES PYRÉNÉES, FRANCE).—Mild Sulphurous. Helium is given off by the water—due in all probability to radium-containing mineral at the source. Similar to Barèges and Cauterets. Bronchial catarrh, phthisis, neurasthenia, asthma. June 1st to October 1st, and imported.

Has reputation of curing sterility in women. *c.f.* Franzensbad.

**Eilsen** (SCHAUMBURG-LIPPE, GERMANY).—Sulphurous, Calcium Sulphate Sulphuretted Hydrogen, Carbonic Acid. Asthmatic affections, neurasthenia, cardiac asthma, bronchial affections, chlorosis.

**Friesms, Bad-** (GERMANY).—Several springs: Kranchen, Kessel-brunnen Kaiser-brunnen, Victoria, Fuersten-brunnen, Alkaline Saline; rises warm. Sodium, Calcium and Magnesium Bicarbonates, Sodium Chloride, free Car-



bonic Acid Indigestion, asthma, emphysema, gout, useful in coughs with expectoration, and pulmonary catarrh. See also Table of Waters.

**Enghien-les-Bains** (near PARIS).—Sulphurous. Lung and skin affections, uterine disorders, nervous diseases, nose and ear affections. Season, May 1 to Oct. 15. Imported.

**Eridauros** (GRECIAN).—Imported.—Ph. Notes.

\* **Esvach**.—Aperient. Magnes. Sodium and Potassium Sulphates and Bicarbonates, free Carbonic Acid. Habitual constipation, indigestion, biliousness, gout. Bottled.

**Evian-les-Bains** (HAUTE SAVOY) Sources "Cachat" and La Croix.—Alkaline table water. Calcium and Magnesium Bicarbonates, free Carbonic Acid. Liver and intestinal disorders. For washing out bladder in uric acid troubles; calculi, cystitis May to October. See also Table of Waters.

**Fachingen** (NASSAU, GERMANY).—Alkaline Acidulated. Bicarbonates of Alkalies and Alkaline earth metals. Said to be bacteriologically pure. In infectious diseases, *e.g.*, typhoid, cholera, also for use in the tropics in malaria, and for intestinal diseases. gastric catarrh, heartburn, uric acid, rheumatism, diabetes, nephritis.

**Fango Mud Springs** (ITALY).—Installation at Matlock. For the treatment of rheumatism.

**Fiuggi** (ITALY).—Saline. Sodium Chloride, Potassium Nitrate, Calcium Carbonate, Carbonic Acid, Ozone, and Oxygen (possibly due to action of radium emanations contained), Nitrogen. Gastric complaints. Imported. Full report on.—L. ii./07 915.

**Flitwick** (near AMPHILL, BEDFORDSHIRE).—Ferruginous Ferric Persulphate and Sodium Sulphate. Anæmia, chlorosis, dyspepsia, general debility and neuralgia. Bottled.

**Folkestone** contains about  $2\frac{1}{2}$  to 3 grains of chalk per pint—if boiled about  $\frac{1}{2}$  grain—which cannot be considered deleterious or have any bad effect. Folkestone water is exceedingly pure containing a trace only of Free Ammonia and 0.0008 grain per gallon of Albuminoid Ammonia. Total Hardness 18.7. Permanent Hardness 2.9 grains per gallon. Constipation is often produced by a visit to seaside towns. It is claimed that this is more likely due to climate and change than to effect of the water. Constipation is common amongst sailors who drink condensed water—it cannot in this case be ascribed to chalky water.—B.M.J. i./11 1430; L. i./11, 1642 ii./11 158.

\* **Fontalis**.—A pure table water. Alkaline. Chlorides and Carbonates, free from Lime and Magnesium Salts. Bottled at Harrogate.

**Forges** (NORMANDY).—Chalybeate. Ferrous Bicarbonate. Chlorosis, dyspepsia. Season, June 1st to October 1st. Imported.

**Franzensbad** (BOHEMIA).—Aperient, Alkaline, Ferruginous. Intestinal catarrh, enlarged liver and spleen, Bright's disease, gout, scrofula, anæmia, general debility, diabetes.

Has been recommended in heart affections. Has powerful effect on the blood, mucous membranes, and nervous system.—M.P., Sept. 23./08, 338.

Enjoys a reputation of curing sterility in women. Thyroid secretion is thought to be evoked.—B.M.J. ii./09, 1265.

\* **Franz Joseph** (BUDA-PESTH, HUNGARY).—Aper. Magnesium, Calcium and Sodium Sulphates. Carbonic Acid. Habitual constipation, diseases of the liver, for piles, biliousness, headache, catarrh of the stomach and intestines. See also Table of Mineral Waters.

\* **Friedrichshall** (SAXE-MEININGEN, GERMANY).—Aperient, Magnesium and Sodium Sulphates, Sodium Chloride, Magnesium Chloride. Constipation, intestinal complaints, biliary disorders, gallstones, gravel, gout, scrofula; an active diuresic and for hæmorrhoids. See also Table of Mineral Waters.

**Gastein, Bad-** (AUSTRIA).—Very slight mineral content. Suitable for weak digestion, nervous disorders, paralysis, uterine affections. Imported.

**Geilnau** (GERMANY).—Alkaline table water.

\* **Gerolstein** (PRUSSIA).—Alkaline. Antacid.

**Giesshubler** (bei KARLSBAD, BOHEMIA).—Alkaline acidulated table water. Sodium, Potassium, Magnesium and Lithium Bicarbonates, free Carbonic Acid. Intestinal catarrhs, dyspepsia, heartburn, hæmorrhoids and gout.

**Gilgit** (KASHMIR, INDIA).—Goitre does not occur among the coolies who drink the pure water of the Gilgit river. Total solids 7 grs. per gall. Total Hardness 4, Calcium about 6, free ammonia and organic matter nil.—L. ii./06, 1570.

**Godesberger** (GERMANY).—Table water. Alkaline, Saline, Chalybeate.  
**Grassion** (FRANCE).—Bituminous. Throat and chest affections, gastric and vesical catarrh. Imported.

**Griesbach** (GERMANY).—Tonic ferruginous table water. Iron Carbonate, Sodium Sulphate, Calcium Carbonate.

Ⓔ **Guber** (SREBRENICA, BOSNIA).—Chalybeate. Contains Arsenious Acid. Anæmia, skin and nerve affections.

**Gytje**—A kind of mud from the Norway fjords used in the "Gytje" treatment in balneology for gout and rheumatism.—Ph. Notes.

**Halle** (BAVARIA).—Saline Bromo-iodised. Goitre, scrofulous swellings. Imported.

**Harrogate** (YORKSHIRE).—Sulphurous. Skin and rheumatic affections, anæmia, dyspepsia. Aperient and diuretic. Summer and winter, and bottled. The Sulphur and Alkaline Carbonates compose half the solid ingredients. The Beckwith Spring contains large proportion of Magnesia. Helium has been traced in the gases rising, hence presence of Radium is assumed.—P.J. i./05,903.

Some pharmacological effects of the strong sulphur **Harrogate** water. :—

A daily excess of urination was observed amounting to 42% when comparing two periods — 11 days without and 11 days with. Similarly weight of fæces showed an increase of 245%. Total Nitrogen showed increase of 8%, Uric Acid 18%, Kreatinin 14%, Phosphates 10%. There is increased oxidation and tissue change, and general metabolism is greatly influenced. In some cases of gout the diminution of amount of urine passed (often under 20 ounces in 24 hours) is rapidly relieved—the diuresis amounting to over 100% and the sp. gr. of the urine does not vary inversely as the amount passed. Indeed, the sp. gr. is often highest at the height of the diuresis.—D. Brown. B.M.J. i./11,1304.

In a previous paper by the same author (B.M.J. ii./10,421) analogous conclusions were given. It may be added from this that exogenous purins excreted are increased. Excretion of endogenous Xanthin bases is decreased.

Sulphuretted Hydrogen content is 10·46 cubic inches per gallon.—B.M.J. ii./11,522.

Eczema, psoriasis, lupus erythematosus, furunculosis, urticaria, etc., treatment of, by the waters and baths at Harrogate.—B.M.J. ii./13,1019.

"**Harrogate Salts**."—Potassium Tartrate 360 grains, Magnesium Sulphate 1 pound, Sulphurated Potash 1 ounce.—P.J. i./07,548.

**Hathorn** (see SARATOGA).

**Homburg von der Höhe** (GERMANY).—Elizabeth-brunnen, Kaiser-brunnen and Stahl-brunnen. Saline chalybeate, acidulated. Sodium and Magnesium Chloride, Ferrous, Calcium and Magnesium Bicarbonates, Carbonic Acid. Chronic catarrhs of stomach and bowels, habitual constipation, gout, scrofula, chlorosis, inaction of the liver, diabetes and general tonic.

\* **Hunyadi Janos** (BUDA-PESTH).—Aperient. Large percentage of Magnesium and Sodium Sulphates, Sodium Chloride, and Sodium and Calcium Bicarbonates. See also Table. Constipation and biliousness. Imported.

**Hypate** (GRECIAN).—Sulphurous. Imported.—Ph. Notes.

**Igmandi** (KOMAROM, HUNGARY) Water. Radio-active. Saline aperient. Magnesium Sulphate 29·3, Sodium Sulphate 9·5, Calcium Sulphate 0·7, Sodium Chloride 0·8%. Total solids 40·8 per 1,000 Gm. Radio-activity inherent in the Calcium Sulphate.—L. ii./05,777. Corpulency, constipation, hæmorrhoids, rheumatism.

**Iodbad Lippik**. See Lippik.

**Ilkley and Ben Rhydding** (ILKLEY in WHARFDALE). Chalybeate and Antacid. (i.) Chalybeate Spring. Ferrous Carbonate, Calcium Sulphate, and Alkaline Chloride. (ii.) "Hygeia" Spring. Calcium, Sodium and Magnesium Carbonates, Sodium Sulphate. (iii.) "Ilkley Wells" Carbonated. Free Carbonic Acid Calcium Carbonate, Sodium Sulphate, Gout and rheumatism. See also **Health Resorts**.

**Johannis** (HESSE-NASSAU).—Saline acidulated tonic table water. Calcium, Magnesium and Sodium Bicarbonates, and Sodium Chloride. See also Table. Imported.

**Kaiser Brunnen** (AIX-LA-CHAPELLE).—Table water. Sodium Chloride, Bicarbonates. Gout, rheumatism and dyspepsia.

**Kissingen** (BAVARIA, GERMANY), **RAKOCZY** and **PANDUR**.—Saline, Chalybeate, Sodium and Potassium Chlorides, Iron and Calcium Bicarbonates



Anæmia, general debility, mental exhaustion, heart, liver, and kidney diseases; gout, obesity, and congestions. Imported.

**Kissingen (BAVARIA) BITTER WATER.**—Aperient, Magnesium and Sodium Sulphates, Carbonic Acid.

**Koenigsdorf (OBERSCHLESIEEN, GERMANY).**—Alkaline Iodised. Sodium Chloride, Calcium Chloride, Magnesium Iodide and Magnesium Bromide. To improve blood condition, for nerve and uterine diseases, glandular swellings and skin affections.

**Krankenheil (BAVARIA).**—Sulphurous, Iodised. Sodium Chloride, Iodide and Bromide, Sulphuretted Hydrogen. Goitre and similar swellings, skin affections.

**Kreuznach (PRUSSIA).**—Iodised Saline. Sodium, Calcium, and Magnesium Chlorides, with small quantity of Bromides, Iodides. In syphilis, tabes, phthisis, obesity, anæmia, skin and nervous disorders, goitre, and similar swellings. All the year round. Imported. Kreuznach mother lye contains 3,100 grains of Salts in 20 ounces.—P.J. ii./04,136.

Radio-active substances obtained from residues of these springs. Used in rheumatism, neuralgia and sciatica. —L. i./09,1283.

Has a reputation of curing sterility in women. *c.f.* Franzensbad.

**\*Kristaly (at ST. LUCASBAD, BUDA-PESTH).**—Table water. Magnesium and Calcium Bicarbonates, Carbonic Acid. In intestinal disorders.

**Krondorf (bei CARLSBAD).**—Alkaline, table water. Chronic catarrh of respiratory tract, also jaundice, gout and allied disorders.

**\*Kronen-Quelle (OBERSALZBRUNN, SILESIA).**—Alk., Saline Lithiated. Sodium Sulphate, Potassium Sulphate, Bicarbonates of Sodium, Magnesium, Calcium, and Lithium. Uric acid diathesis. Imported.

**\*Kronthal (NASSAU).**—Saline, table water. Sodium Chloride, Calcium Carbonate. BLUE LABEL.—Plain table water and for dyspepsia. RED LABEL.—Pick-me-up, rheumatism, gout. GREEN LABEL.—Anæmia and tonic.

**Kyllini (GRECIAN).**—Sulphurous. Imported.—Ph. Notes.

**Kythnos (GRECIAN).**—Saline, Thermal. Imported.—Ph. Notes.

**Labassère (HAUTES PYRÉNÉES).**—See Bagneres de Bigorre.

**Landeck, Bad Landeck (PRUSSIAN SILESIA).**—Sulphurous. Nervous, skin and rheumatic disease. Moo-baths.

**Langenbrücken (BADEN).**—Alkaline, saline. Sulphurous. Chronic skin diseases, syphilis, rheumatism, gout, bronchial catarrh.

**La Preste (EASTERN PYRENEES** about 50 miles from Perpignan).—In affections of the urinary tract—cystitis, vesical catarrh, prostatitis, etc. Contains only 11·2 grains per gallon total solids. Silica one of the leading constituents.

**Latraki (GRECIAN).**—Alkaline.—Ph. Notes.

**Leamington.**—Saline. Calcium, Magnesium, Strontium and Barium Sulphates, Sodium, Calcium, Magnesium and Potassium Chlorides, Magnesium Bromide and Iodide, Calcium and Iron Carbonates with traces of Manganese and Titanium.—S. H. Smith, 1914. Dyspepsia, gout, women's diseases, sciatica, glandular swellings and skin diseases. Bottled. See also Table.

**⑧ Levico (AUSTRIAN TYROL).**—Two springs (strong and mild); Arsenical chalybeate. STRONG: Arsenious Acid; 0·09 part per 10,000—1·12th of a grain per pint; the MILD is 1·10th of this. Further constituents: Ferrous Sulphate, and Ferric Persulphate. Anæmia, skin eruptions, neuralgia and amenorrhœa.

**Lippik (SLAVONIA, HUNGARY).**—Iodised water and acidulated. Potassium and Sodium Sulphates, Sodium Chloride, Sodium Iodide, Sodium Bicarbonate. Stomach diseases, scrofulosis, rheumatism, gout, glandular swellings.

**Lippspringe (WESTPHALIA).**—Alkaline, acidulated. Chronic lung affections, intestinal and bone diseases.

**Llandrindod (WALES).**—"Strong Sulphur," "Roman Spring," "Magnesium Spring." The first is radio-active. In skin affections, dyspepsia, glandular enlargements, gout, rheumatism. Season all the year round.

The Sulphuretted Hydrogen waters are of several strengths. One contains a small amount of thallium chloride and a considerable quantity of lithia—latter higher than Royat.—B.M.J. i./09,1245.

**Llangammarch.**—See Barium.

**Llanwrtyd, Dolecoed Spa (WALES).**—Sulphuretted Hydrogen, the strongest in Great Britain.

**Louche (Leuk or Loeche les Bains) (VALAIS, SWITZERLAND).**—Warm, almost exclusively for baths. Calcium Sulphate, Magnesium Sulphate, similar

to that of Bath in England. Rheumatism, gout, women's diseases, skin affections. 1st May to 15th October.

**Luhatschowitz (AUSTRIA).**—Saline, with small quantities of Bromides and odides. Catarrhal affections, gouty exudations. Imported.

\***Lullus, (St. HERSFELD, HESSE, Germany).**—Glauber's Salt principal constituent. Stomach, liver, bowel complaints.

**Magnaris.**—A table water prepared at Llandrindod.

**Malvern (WORCESTERSHIRE).**—Practically free from saline matter, and contains no organic matter. Bladder and kidney diseases and skin affections. Bottled. See also Table.

\***Malvern Selzer.**—Slightly saline table water.

**Marcols (ARDÈCHE, FRANCE), Source du Lion.**—Alkaline table water. Stomach, liver and kidney diseases, rheumatism. Imported.

**Marienbad (BOHEMIA).**—Several springs, Kreuz-brunnen and Ferdinand-brunnen principal, Alkaline, Saline, Chalybeate, Acidulated. Gout, gravel, hæmorrhoids, brain and nervous diseases, melancholia and chronic gastric catarrh, dyspepsia, gall stones, obesity. Also supplied in powder and crystals. Tablets are also made. See Marienbad Salt and Table of Waters.

**Martigny (VOSGES).** Lithiated. Gravel, diabetes, liver and kidney complaints.

**Mergentheim (WURTEMBERG), Karlsquelle.**—Aperient Water. Magnesium and Sodium Sulphates, Sodium Chloride, free Carbonic Acid. Gout, neuralgia, gall stones, dyspepsia, obesity, rheumatism, diabetes.

**Meritchleri (BULGARIA).**—Water resembles Carlsbad.—B.M.J. ii./07, 536.

**Methana (GRECIAN).**—Sulphurous.—Ph. Notes. So powerful as to render the place objectionable; the sea into which the water falls is milky, owing to the decomposition of the sulphuretted hydrogen. The bacterium *Beggiatoa nivea* is found in the sediment, and in the protoplasm of this organism particles of sulphur are distinctly visible under the microscope. Imported.

**Metternich (BOHEMIA).**—Alkaline table water.

**Miers (LOT, FRANCE).**—Saline, laxative. Sodium Sulphate, Calcium Sulphate, Magnesium Chloride. Dyspepsia, calculi, migraine, obesity, albuminuria. Imported.

**Missisquoi (VERMONT, U.S.A.).**—Sulphurous. Scrofula and other skin affections, diseases of respiratory organs. Imported.

**Mondorf (LUXEMBOURG).**—Saline. Calcium Chloride, Bicarbonates, with small quantity of Magnesium Bromide. Constipation, neurasthenia, anæmia, skin affections, jaundice, rheumatism. Imported.

⑩ **Mont Dore (PUY DE DÔME, FRANCE).**—Alkaline, Saline. Bicarbonates, Ferrous Carbonate, Arsenic, and Silica. Intestinal disorders, rheumatism, asthuma, bronchitis and laryngitis. June 1st to September 20th. Imported.

**Montreux (SWITZERLAND).**—Alkaline table water. Slightly mineralised. Stomach, liver, kidney and bladder affections. Imported.

**Nauheim (GERMANY).**—Sodium, Calcium and Lithium Chlorides. Skin and rheumatic affections, heart diseases. See also Table of Waters.

**Neenndorf (WESTPHALIA).**—With mud baths. Sulphurous, Calcium Sulphurate, Magnesium Sulphate, Carbonic Acid, Sulphuretted Hydrogen. Claimed to be the strongest sulphurous water in Europe. Rheumatism, neuralgia, skin and bronchial affections, hæmorrhoids, neurosis, &c.

**Neuenahr (PRUSSIA).**—Acidulated, alkaline table water. Laryngitis, bronchial catarrh, asthma, tuberculosis, liver diseases, diabetes, heart disease, diuretic.—L. ii./09, 1276. Imported as Apollinaris.

**Nieder Selters.**—See Selters, Nieder-.

**Nocera Umbria (Angelica Spring, 185 kilometres from ROME).**—Alkaline, Bicarbonates, Digestive, anturic, tonic refreshing. Imported.

**Orezza.**—See D'Orezza.

**Oberbrunnen (SILESIA).**—Alkaline Lithiated. Uric acid diathesis, nephritis.

\***Perrier (VERGESE nr. NISMES, FRANCE).**—Table water, slightly mineralised, organically pure. Small proportion of Alkaline Carbonates. Digestive. M.P., June 22/04.

⑪ **Plombières (VOSGES, FRANCE).**—Mild Saline. Sodium Sulphate, Arsenic, Oxygen, Nitrogen. Neurasthenia, gastralgia, dyspepsia, dilation of the stomach and chronic diarrhoea, rheumatism, skin affections. May to September. Imported. Mucous colitis treated by washing out the colon with the alkaline sulphur water and further bath treatment.—B.M.J. ii./08 78. Radioactive.—Chem. News, Mar. 1, 08, p. 132.



**Pöstyén** (BAD PÖSTYÉN, HUNGARY).—A few miles from Vienna. Hot springs with temperature  $140^{\circ}$  F. Sulphurous Radioactive. Thermal Mud Immersion baths. Rheumatism and Gout.—Pr., Mar., 1912, 488.

**Pougues** (FRANCE).—St. Leger Spring.—Alkaline. Dyspepsia, anæmia, scrofula, gravel, catarrh of the bladder. May 15 to Sept. 30. Imported.

**Pullna** (BOHEMIA).—Aperient. Magnesium, Sodium and Potassium Sulphates, Sodium Chloride. Chronic constipation, liver and intestinal affections gallstones, gout and rheumatism, eczema.

**Pyrmont** (WALDECK, WESTPHALIA). Three springs. HAUPTQUELLE contains most iron.—Chalybeate. Chronic catarrh, digestive and urinary diseases, women's diseases, scrofula, rheumatism and gout.

**Quicherat** (FRANCE).—Ferruginous. Magnesium and Sodium Chlorides, with some Iron and Manganese, Carbonic Acid. Anæmia, stomach diseases. Imported.

**Ragatz-Pfäfers**.—Canton St. Gall, Switzerland. Thermal Spring  $99^{\circ}$  Fahrenheit. Calcium, Magnesium, and Sodium Chlorides, Bicarbonates, and Sulphates. Very free from bacteria. Rheumatism, gout, sciatica, neuralgia. May to October.

**Recoaro** (VENETIA, LOMBARDY). Sources: Lelia, Lorguia and Giuliana.—Ferruginous Table Waters. Sulphates. Intestinal and liver complaints. Tonic, easily assimilated. Summer and imported. ROYAL BITTER SOURCE.—Is pure bacteriologically. Purgative for intestinal complaints.

**Reichenhall** (BAVARIAN ALPS).—Saline. Considerable proportion of Sodium Chloride. Employed principally as bath in scrofula and given for bronchial catarrh.

**Rennine** (REIPERTSWEILER, ALSACE).—Nitrated. Potassium Nitrate 0.19 Gm. per litre, Alkaline Chlorides. Diuretic, laxative, in heart disease.—L. ii./03,107.

**Renaison** (FRANCE).—Alkaline, acidulated table water. Bicarbonates, free Carbonic Acid. Dyspepsia and gastric disorders. Imported.

**Rhens** (AM RHEIN, GERMANY).—Alkaline, acidulated table water. Sodium Chloride, Sulphate and Bicarbonate. Imported.

**Rippoldsau** (BADEN).—Saline, Acidulous, Chalybeate. Calcium Bicarbonate, Manganous and Ferrous Bicarbonates, Sodium Sulphate, free Carbonic Acid. Anæmia, scrofula, skin affections, rheumatism, gout, neuralgia.

**Rosdorf** (PRUSSIA).—Alkaline, saline, acidulated table water. Easy of digestion, for catarrhs of stomach and intestines, and of respiratory organs, liver and spleen affections and calculi in the bladder.

① **Roncegno** (VALSUGANA, SOUTHERN TYROL).—Each litre contains 0.109 Gm. Sodium Arsenate, 0.115 Gm. Arsenic Anhydride, 0.03 Ferric Phosphate 3.12 Gm. Ferric Sulphate, also Sulphates of Copper, Magnesium Nickel and Cobalt.

Has the highest content of Arsenic in any spring, viz., 42.6 mgr.  $As_2O_3$  per litre.—P.J. i./12,689.

In addition to 0.007%  $As_2O_5$ , O. Bennett found 0.004% Antimony Oxide.—P.J. ii./12,286.

Graves' Disease, 20 out of 37 cases completely cured.—B.M.J. ii./09,992.

**Rosbach** (near HOMBURG, GERMANY).—Saline, table water. Calcium and Magnesium Bicarbonates, Carbonic Acid. Gouty and acid dyspepsia.

② **Royat** (PUY-DE-DÔME, FRANCE). Three Springs.—Saline, Arsenated [small quantity], Lithiated. Rheumatism, dyspepsia, nervous diseases, women's diseases, anæmia, skin affections and debility. Summer. Imported. Full description of this water.—B.M.J. i. 07,758.

**Rubinat** (PYRÉNÉES, SPAIN). "Llorach" Spring.—Aperient. Rich in Sodium Sulphate and Magnesium Sulphate, and contains Calcium Chloride. Stomachic disorders, constipation, liver and kidney affections. Imported. See also Table of Mineral Waters.

**Rubinat** (SERRE).—Similar to the last mentioned, but stronger than the above in the proportion of Sodium Sulphate to Magnesium Sulphate. Uses similar to the above. Imported.

③ **Saint Boès** (BASSES-PYRÉNÉES, FRANCE).—Bituminous, Iodised, and Arsenated. Arsenic, Iodine. Skin, lung, and venereal diseases. Imported.

**Saint Galmier** (LOIRE, FRANCE).—"Badoit" Table water. Dyspepsia, intestinal catarrh, constipation, nervous disorders, hyperæmia. Imported. "Noël."—Alkaline, Acidulated. Uses as latter. Imported.

**Saint Gervais** (HAUTE SAVOIE).—Saline. Sodium and Calcium Sulphates, Sodium Chloride. Skin affections, constipation, rheumatism and nerve diseases. 15th May to 30th September. Imported.

\***Saint Lucasbad Brunnen** (BUDA-PESTH).—Sulphurous. Rheumatism neuralgia, and skin affections. See also BUDA-PESTH.

**Saint Moritz** (SWITZERLAND). “Paracelse” Spring.—Alkaline, Chalybeate, Tonic. Nervous and intestinal disorders, sick headache, hysteria, Graves’ disease and for convalescence. All the year round. Imported.

**Saint Sauveur**.—See **Vernet les Bains**.

**Salies de Bearn** (FRANCE).—Saline. Sodium Bromide and Iodide. Skin affections and as a general tonic.

**Salins les Bains** (JURA, FRANCE).—Tonic. Magnesium Chloride, Iodides and Bromides. Anæmia, tuberculosis, general debility, women’s diseases, obesity, and scrofulous affections. Summer. Imported.

**Sallyco**.—Artificial. Is stated to contain Colchiçine and Salicylic Acid.

\***Salutaris**—Still and aerated table water, distilled water. For washing out the system in kidney and liver disorders, also gout and dyspepsia.

\***Salvator Forras** (HUNGARY).—Alkalihe, Lithiated. Uric acid diseases of digestive organs.

**Salzbrunn** (AUSTRIA).—Alkaline. Chronic intestinal diseases, gall stones rheumatic affections, emphysema.

**Salzschlirf**—See **Bonifacius**.

**San Pellegrino** (near MILAN).—Diuretic Calcium and Magnesium Sulphates, some Carbonate with trace of Chloride, also Lithium. Mineral Salts amount to 1.264 Gm. per litre.—L. i./09,43.

**Saratika** (AUSTERILTZ, MORAVIA, HUNGARY).—Purgative. Gout, rheumatism and obesity.

**Saratoga** (U.S.A.). “Congress” and “Hathorn” springs.—Alkaline, Saline. A mild aperient in dyspepsia, skin affections, diseases of the stomach, liver, kidney, and blood, constipation. Imported.

**Sauerbrunnen** (HARTZ, GERMANY).—Table water. Very slight mineral constituents—Magnesium Carbonate and Sulphates. Imported.

**Schinznach** (SWITZERLAND).—Sulphurous. Skin affections (eczema, acne, psoriasis, urticaria), asthma, gout, rheumatism. Has reputation of curing sterility in women. *c.f.* Franzensbad.

**Schlangenbad** (GERMANY).—Very slight Mineral constituents. Considerable quantity of dissolved oxygen and nitrogen. General tonic.

**Schwalbach** (NASSAU). Weinbrunnen and Stahlbrunnen—Chalybeate tonic. Iron, Calcium and Magnesium Bicarbonates. Anæmia, and as a tonic.

**Selters, or Seltzer Water** (on the LAHN, NASSAU), OBER and NIEDER.—Alkaline, Acidulated, Table Water. Sodium Chloride, Bicarbonates, Carbonic Acid. Dyspepsia, obesity, gout, rheumatism, bronchial, bladder, kidney and liver affections.

**Slanic Spa** (ROUMANIA).—Rich in Carbonic Acid, Alkaline. Stimulates secretion by content of Sodium Chloride. Neutralises excess of Hydrochloric Acid by the alkali (Sodium Bicarbonate).—B.M.J.E. i./11,40.

**Soulac-sur-Mer** (MEDOC, GIRONDE, FRANCE).—Health resort. Sea air.

**Spa** (BELGIUM).—Ferruginous. Anæmia, uterine and nervous disorders rheumatism, gout. Summer, and imported.

**Strathpeffer**.—See British Health Resorts.

\***Sulis** (Bath Water, aerated).—Aperient table water. Calcium and Sodium Sulphates, Magnesium and Sodium Chloride. Gives a radio-active emanation.

**Tarasp** (SWITZERLAND). St. Lucius Spring.—Alkaline, Saline. Diuretic. Useful in chronic catarrh of the stomach, dyspepsia, gastralgia, habitual constipation, disorders of nutrition, obesity. 1st June to 15th Sept. Imported.

**Taunus** (FRANKFURT).—Muriate, alkaline table water. Digestive. \***Taunus Mineral Water**.

**Teplitz** (BOHEMIA).—Alkaline. Rheumatic and nervous diseases, paralysis.

**Tonalka**. An alkaline tonic aperient water. Supplied in syphons and bottles.



**Thonon** (LAKE LÉMAN, FRANCE). Alkaline, Carbonated and Benzoated (Balsamic resins are contained). In liver complaints and urinary diseases. Imported bottled.

**Tsagesi** (GRECIAN). Chalybeate.—Ph. Notes.

**Uriage**.—Waters considered to facilitate absorption of Mercury.—D. Freshwater, Pr., Mar., 1912.

**Vals** (ARDÈCHE, FRANCE). Springs: Madeleine, Précieuse, Désirée, Rigollette, St. Jean.—Alkaline, acidulated. (Contents vary with the spring.) Rheumatism, anæmia, skin affections. Imported.

**Vernet-les-Bains** (PYRÉNÉES ORIENTALES).—Sulphate. Sodium Sulphate and Thiosulphate. Constipation, skin affections, anæmia. May to October, and imported.

★ **Vichy** (ALLIER, FRANCE). Springs: Grande Grille, Hôpital, Célestins, Parc.—Alkaline, acidulated. Gravel, chronic urinary affections, diabetes, female complaints, gout, rheumatism, facilitates digestion. May 15th to September 30th, and imported.—M.P., Aug. 26, 1903.

For renal elimination but does not appeal to English visitors.—L. ii./09, 1276.

**Villacabras** (SPAIN).—Saline aperient. Sodium Sulphate. Obesity and constipation. Imported.

**Vittel** (VOSGES, FRANCE). Spring: Grande Source.—Alkaline. Sodium and Magnesium Bicarbonates, Sodium, Calcium, and Magnesium Sulphates Carbonic Acid. Uric acid, scrofula, chlorosis, biliary and urinary congestion. In addition are Source Salée, stronger in Magnesium Sulphate; Source Marie and Source des Demoiselles, Chalybeate. The first two are imported.

Aortitis relieved, pain becoming less frequent. Dyspnœa practically disappeared by a course at Vittel.—B.M.J. ii./08, 80.

**Weilbach** (NASSAU).—Alkaline, Sulphurous. (A lithiated spring also.) Aperient, for obstructions of the abdominal organs, antisypilitic, in lung and skin diseases.

**Wiesbaden** (NASSAU). Kochbrunnen.—Antacid. Uric acid affections, sciatica, bronchitis and laryngitis.

**Wildbad** (BLACK FOREST, GERMANY).—Alkaline. Warm (37° C.). Rheumatism, paralysis, neuralgia, scrofula, rickets, bronchial catarrh, urinary diseases.

**Wildungen** (WALDECK, GERMANY). Three Springs.—Alkaline. Bladder and urinary diseases, anæmia.

**Wittekind** (HALLE, GERMANY).—Sodium Sulphate. Obesity, women's diseases, rheumatism, heart and nerve diseases.

⑩ **Woodhall** (LINCOLNSHIRE).—Saline, Bromo-iodised. Bromide, Iodine (free and combined), Sodium Chloride, Arsenic. Gout, sciatica, rheumatism, skin affections, goitre, women's diseases.

A large range of diseases from arthritis to eczema may be treated on orthodox principles.—L. i./09, 1478.

★ **Wychia** (DROITWICH).—Saline. Sodium Chloride 11·93 and Sodium Sulphate 7·89 per litre. Droitwich water is distinctly radio-active. Laxative, habitual constipation and plethora.—L. i./06, 38.

*Droitwich Brine Baths have no equal for treatment of sciatica and allied affections. Even rheumatoid arthritis is certainly improved and in some cases actually cured. The cures of chronic sciatica are most striking.*

*Analysis of the brine has shown it to contain 20,000 grains per gallon of saline constituents in excess of that possessed by any other known water. The actual figures are: Chloride of Sodium, 21761·8; Chloride of Magnesium, 2·5; Sulphate of Lime, 91·1; sulphate of Alumina, 14·4; Sulphate of Soda, 342·7; Iodide of Sodium, 0·208; total salts to an imperial gallon, 22212·8.*

*The brine acts possibly by absorption through the skin because the acidity of the urine is diminished, the output of uric acid being eventually lessened. Patients soon remark the change of colour in their urine, and the absence of pink deposit so well known in lithæmia. Urates are increased at first, and afterwards, as the urine becomes alkaline, they become diminished. The brine acts as a powerful uric-acid solvent. The radium emanation contained has something to do with this. Wonderful results in neurasthenia. Certain diseases are aggravated by the brine, e.g., malignant disease. The brine will cure almost every variety of uric-acid disease, both those belonging to the collemic, and also to the arthritic group.—Jl. R.A.M.C., July, 1911.*

## A Table of certain Mineral Waters showing their Approximate Contents in Grains per Pint.

In the following Table we have arranged a brief list of some of the waters, giving their principal constituents from various published analyses. It occurred to us that an arrangement of this kind would be of interest as enabling the physician to see at a glance the relative *proportions of the various main elements* and the forms in which they occur in the waters. The Salts showing the higher quantities take precedence in each column.

SPRING.	CHARACTER.	CARBONATES (more or less in form of Bicar- bonates).	CHLORIDES.	SULPHATES.	OTHER CONSTITUENTS and authority.
Æsculap	Saline Aperient.	Sodium, 8½	Sodium, 25½.	Magnesium, 151½ Sodium, 121½. Calcium, 18½. Sodium, 2½. Potassium, 1½.	Traces of Alumina, Iron, Man- ganese.—J. Molnar.
Aix-la-Cha- pelle.	Saline Sulphurous.	Sodium, 6½. Calcium, 1½. Magnesium, ½.	Sodium, 25½		Traces of Sulphides, Iodides and Bromides, Lithium, Iron and Strontium.— Baron Liebig.
"Kaiser Brunnen).	Table Water	Sodium, 8. Calcium, 2. Magnesium, ½.	Sodium, 23.	Sodium, 2½. Potassium, 1½.	Sodium Sulphide ½. Traces of Iodide, Bromide, Lithium, Strontium, Iron.
Apenta	Saline Aperient.	Sodium, 4. Magnesium, 1½. (Calcium, 1. Ferrous, ½.	Sodium, 15½.	Magnesium, 184½. Sodium, 164. Calcium, 23. Potassium, ½. Lithium, ½.	Traces of Bromide Alumina, etc.—R. C. Tichborne.
Apollinaris	Table Water.	Sodium, ½. Magnesium, 3½. Calcium, 2½.	Sodium, 3½.	Sodium, 2.	CO <sub>2</sub> (Free) 24½.—Apol- linaris Co.



SPRING.	CHARACTER.	CARBONATES (more or less in form of Bicar- bonates).	CHLORIDES.	SULPHATES.	OTHER CONSTITUENTS AND AUTHORITY.
Bath	Table Water.	Calcium, 1.	Magnesium 2. Sodium, 2.	Calcium, 11½. Sodium, 3. Potassium, 1.	Traces of Iron, Ammonia, Nitrates. See also p. 170.
Buxton (St. Anne, Ther- mal)	Slightly saline gas- eous table water.	Calcium, 1½. Magnesium ¾.	Sodium, ½. Ammonium, ¼. Magnesium, ¼.	Sodium } Potassium } Calcium }	Traces of Iron, Manganese and Barium, Sulphates. See also p. 171.
Buxton (Chalybeate)	Chalybeate.	Ferrous, ½. Magnesium, ¼.	Sodium, ½.	Calcium, 1½. Magnesium, ½. Sodium ¼.	Traces of Aluminium and Potassium Salts.
Carlsbad (Sprudel)	Alkaline.	Sodium, 11½. Calcium, 3. Magnesium, 1½	Sodium, 9.	Sodium, 21. Potassium, 1½.	Traces of Lithium, Stron- tium, Aluminium and Fluorine Compounds.— Prof. E. Ludwig and J. Mauthner.
Cheltenham	Saline Aperient	Calcium, 4½.	Sodium, 3.	Magnesium, 14½. Calcium, 8. Sodium, 7½. Potassium, ½.	Traces of Alumina, Iron, Manganese, Bromides, Io- dides, Phosphate.
Condal	Aperient	—	Sodium, 16½.	Sodium, 390½. Magnesium, 27. Calcium, 14½. Potassium, 4½.	Traces of Alumina, Iron.— Ecole Nat. des Mines, Paris

SPRING.	CHARACTER.	CARBONATES (more or less in form of Bicar- bonates).	CHLORIDES.	SULPHATE.	OTHER CONSTITUENTS AND AUTHORITY.
Contrexé- ville (Pavillon)	Alkaline.	Calcium, 3½. Magnesium, ¼.	—	Calcium, 13¼. Sodium, 2. Magnesium, ¼.	CO <sub>2</sub> ¾; (Le Cler Spring 10)., Traces of Arsenic, Chlorides, Fluorides.
Ems (Kränchen)	Alkaline Saline.	Sodium, 8½. Calcium, 2. Magnesium, 1¾.	Sodium, 8¾.	Potassium, ½. Sodium, ¼.	CO <sub>2</sub> and traces of Alumina Barium, Iron, Manganese, Strontium, Phosphate.— Fresenius.
Evian-les- bains (Cachat)	Alkaline.	Calcium, 1¾. Magnesium, ¾.	—	—	CO <sub>2</sub> and traces of Iron Magnesium, Sodium, Chlor- ide, Nitrate, Phosphate.— Willm, Lille.
Franz Josef.	Aperient.	—	Magnesium, 14½.	Magnesium 216¼. Sodium, 211. Calcium, 16¼.	CO <sub>2</sub> 9¼ total. Traces of Alumina, Iron.— Attfield.
Friedrich- shall	Saline Aperient.	—	Sodium, 69½. Magnesium, 43.	Magnesium 54½. Sodium, 45½.	Municipal Chemists of Breslau.
Harrogate <i>vide</i> p 174.	Sulphurous.	—	—	—	—
Hunyadi János	Aperient.	Calcium, 7. Sodium, 6. Strontium, ¼.	Sodium, 15.	Sodium, 197¼. Magnesium, 195½. Potassium, 1.	CO <sub>2</sub> Trace of Iron.—Bunsen
Johannis	Alkaline, Table	Calcium 6½. Sodium, 3¼. Magnesium, 2½.	Sodium, 9.	Sodium, ¼.	CO <sub>2</sub> (Free) 21¼. Traces of Iron, Lithia, Man- ganese and Potash.—H. Plaskuda.



SPRING.	CHARACTER.	CARBONATES (more or less in form of Bicar- bonates).	CHLORIDES.	SULPHATES.	OTHER CONSTITUENTS AND AUTHORITY.
Leamington	Saline.	Calcium, $\frac{1}{3}$ . Iron, $\frac{1}{10}$ .	Sodium, 109. Calcium, 5. Magnesium, 4. Potassium, 1.	Calcium, $21\frac{3}{4}$ . Magnesium, 11.	Lithium, Manganese, Titanium, Iodine, Bromine, S. H. Smith, 1914.
Malvern Vide p. 176	Table.				CO <sub>2</sub> . Lime, Magnesium, Sodium, Chloride, Iodide. (Total = $\frac{3}{4}$ gr. only).
Marienbad (Kreuzbrunnen)	Alkaline chalybeate.	Sodium, $15\frac{1}{2}$ . Calcium, $8\frac{1}{4}$ . Magnesium, $6\frac{3}{4}$ . Ferrous, $\frac{1}{2}$ .	Sodium, 14.	Sodium, $45\frac{1}{4}$ . Potassium, $\frac{1}{2}$ .	Traces of Alumina, Lithia Manganese, Strontium.—Kersten. Ferdinand s-brunnen is a little stronger in Potash and Soda Salts.
Nauheim (Löwenquelle) (Ludwigsbrunnen & Schwalheim are similar)	Non-aperient. Medicinal.	Calcium, $8\frac{1}{2}$ . Magnesium, $3\frac{1}{4}$ . Iron, $\frac{1}{4}$ .	Sodium, $16\frac{1}{2}$ . Magnesium, $\frac{3}{4}$ .	Potassium, $1\frac{1}{4}$ .	CO <sub>2</sub> (Free) $20\frac{1}{2}$ . Traces of Arsenic, Ammonia, Lithium, Manganese, Phosphate
Nauheim Kurbrunnen	Strong Saline Aperient.	Calcium, $11\frac{1}{2}$ . Iron, $\frac{1}{4}$ . Strontium, $\frac{1}{4}$ .	Sodium, 110. Calcium, $9\frac{1}{4}$ . Potassium, $3\frac{1}{4}$ . Magnesium, $2\frac{3}{4}$ . Ammonium, $\frac{1}{4}$ . Lithium, $\frac{1}{4}$ .	Potassium, $\frac{1}{2}$ .	CO <sub>2</sub> (Free) $21\frac{1}{2}$ . Others, <i>vide supra</i> .

SPRING.	CHARACTER.	CARBONATES (more or less in form of Bicar- bonates).	CHLORIDES.	SULPHATES.	OTHER CONSTITUENTS AND AUTHORITY.
Nauheim (Karls- brunnen)	Mild Saline Aperient.	Calcium, 4½.	Sodium, 48. Calcium, 3½. Potassium, 1½. Magnesium, 1.	Potassium, 6½.	CO <sub>2</sub> (Free) 14½. Others, <i>vide antea</i> .
Rubinat (Llorach)	Aperient.	—	Sodium, 18.	Sodium, 844. Magnesium, 28. Calcium, 17.	Traces of Alumina, etc.— Bouchardat.
St. Galmier (Romaines)	Table.	Calcium, 10. Potassium, 8. Magnesium, 7½. Sodium, 6.	Sodium, ½. Calcium, ½. Magnesium, ½.	Calcium, ½. Magnesium, ½. Sodium, ½.	CO <sub>2</sub> (Free) 20½, Alkaline Silicates ½, Traces of Ar- senic, Phosphorus and Iodine. "Badoit" and "Noel" contain about a ¼ and ⅓ respectively of total saline matter of "Romaines."
Vichy (average of the three springs).	Alkaline, Acidulated.	Sodium 2½. Calcium, ½.	Sodium, ½	—	CO <sub>2</sub> ½. Traces of Potassium, Arsenic, Boric Acid, Iron, Manganese and Mag- nesia.
Vittel ('Grande Source')	Sulphated Ferruginous.	Calcium, 1½. Magnesium Sodium } ¼.	Sodium Magnesium Potassium } 2.	Calcium, 4. Magnesium, 3½. Sodium, 3.	Traces of Iodine, Arsenic and Iron.



## BRITISH HEALTH RESORTS.

**Bath.**—Climate mild and equable. Mineral springs. Suitable for gout and rheumatism.

**Ben Rhydding** (*see also Ilkley*).—Bracing. Medicinal springs. Suitable for gout, rheumatism, &c.

**Blackpool** (Lancashire).—Very bracing. During convalescence.

**Bournemouth.**—Mild and dry. Sand and gravel soil. 100 ft. above sea level; protected from N. and E. winds by pine woods. Suits persons coming home from the tropics, and for respiratory diseases.

**Braemar.**—Mountain Health resort. Very bracing climate. Sandy and gravel soil. 1,100 feet above sea level. Suitable for neurasthenia and convalescence from influenza, etc. Season, June to Oct.

**Bridge of Allan.**—Mild and equable. Saline springs. Suitable for consumption, bronchial affections, gout, rheumatism, &c.

**Buxton.**—Highest town in the Kingdom. Thermal springs. Suitable for gout, rheumatism and paralysis.

**Channel Islands** (Jersey, Guernsey, and Alderney).—Climate fine and healthy. Even temperature. Suitable for all pulmonary troubles and neurasthenia.

**Cheltenham.**—Spring, autumn and winter resort. Chalybeate and saline waters. Suitable for respiratory diseases.

**Clifton.**—Climate equable. Alkaline waters. Suitable for respiratory diseases, also diabetes, liver and urinary disorders.

**Cromer.**—Climate very bracing, often too cold in spring; cool in summer. Suitable for anæmia, scrofula, nervous affections, and convalescence.

**Deal.**—Very bracing, pebble beach, not fit for bathing; suitable for rest cure, nervous and chronic cases.

**Droitwich.**—Recommended for its Brine Baths, which are efficacious in rheumatic and gouty affections, congestion of liver and spleen and nervous debility. (*See Wychia Water*).

**Eastbourne.**—Good sea bathing; suited for convalescents from September to January, especially for cases of scrofula and consumption.

**Exmouth.**—The old town high and windy; the new town beside the river and sea beach is more protected, mild and humid.

**Falmouth.**—A warm equable winter climate; a rival to the Riviera, and cool in summer.

**Folkestone.**—Bracing. For Analysis of Water *vide* Mineral Waters.

**Freshwater Bay.**—Isle of Wight. Southern aspect for convalescents and consumptives.—B.M.J. i./o6,990.

**Harrogate.**—Has Sulphur, Chalybeate and other Saline Springs. *See* Mineral Waters.

**Hastings.**—Mild, being suitable as winter resort for convalescents. Many cases of phthisis receive benefit from this climate.

**Ilfracombe.**—Bracing for recovery from illness.

**Ilkley** (*see also Ben Rhydding*).—Bracing moorland air; good fishing; golf links; a hilly district.

**Leamington Spa.**—Equable climate. Saline Springs. Suitable for chronic liver and kidney complaints, dyspepsia and uterine congestion.

**Llandudno.**—Climate bracing and appetising; rather windy; a good place for summer health resort.

**Llandrindod Wells.**—Bracing climate. Thermal waters. Suitable for liver complaint, rheumatism, skin diseases. (*See also Mineral Waters*). 700 feet above sea level.

**Malvern.**—Bracing air; equable climate. Brine and Saline Baths. Suitable in gout, rheumatism, scrofula, &c. (*See also Mineral Waters*.)

**Margate.**—Equable cool temperature, dry sub-soil, and a moderate altitude. Suitable for convalescence and lung complaints, and especially for gland enlargements and tuberculous joints; a very bracing climate.

**Matlock Bath.**—Thermal and Mineral Springs. There is here a Fango di Battaglia (hot volcanic mud cure) installation. Suitable for rheumatic and gouty affections.

**Penzance.**—A mild, equable, warm climate, but not much shelter from winds.

**S Scarborough.**—Exceedingly bracing. Moors in vicinity. Suit nervous hypochondriacal persons and those recovering from illnesses.

**Sidmouth (Devon).**—Climate particularly favourable in catarrhal, bronchial and cardiac affections. In phthisis.—B.M.J. i./o6,990.

**Scilly Isles.**—Mild and humid climate, temperature varying less than at any other watering place in Britain.

**Southport (Lancashire).**—Fine sands, bracing climate, suitable for laryngeal and pulmonary diseases.

**Strathpeffer Spa.**—Strong sulphurous (4 springs, richest in sulphur compounds of any in Great Britain), also an effervescing chalybeate spring. Suitable for rheumatism, gout, liver and skin diseases.

**Torquay (Devon).**—A summer pleasure season, hot and very humid, and a warm winter season; has a mild and equable climate, the soil quickly drying. Suitable for all pulmonary complaints.

**Tunbridge Wells.**—The old town, much sheltered, lies in a warm valley; while houses on the hills around have a bracing climate.

**Ventnor and Weymouth.**—Winter health resorts. Have reputation for phthisical sufferers.

**Weston-super-Mare.**—A mild equable climate; the town sheltered by hills on the north and east; fine sand and plenty of ozone; the tide recedes a great distance.

See also 'MEDICAL DIRECTORY.'—Churchill, London—for further details.

## IRISH HEALTH RESORTS.

**Kingstown, Killiney, Greystones, Bray.**—Mild and dry, comparing with Hastings and Ventnor.

**Tramore, in Waterford.**—Magnificent sandy beach.

**Queenstown.**—A suitable winter health resort, well protected from N. and E. winds.

**Glendore, Glengariff, Parknasilla** are similar.

Sulphuretted water at **Lisdoonvarna** (5'55), **Lucan** (2'7), **Donegal** (8'29), **Ballynahinch** (3'35 Cc. per litre). These are much stronger than Harrogate water in H<sub>2</sub>S.

**Mallow** (70°) is the only warm spring in Ireland.

For several others B.M.J. ii./o7.1583 should be consulted.

See also 'MEDICAL DIRECTORY.'—Churchill, London—for further details.

## Advantages of British Health Resorts for Foreign Invalids.

Hitherto the movement of invalids has been in one direction only. Value of our climatic conditions and maritime resorts.—Neville Wood, Int. Cong. of Med., 1913.—B.M.J. ii./13,542; L. ii./13,809.

## ANTISEPTIC POWER OF NUMEROUS CHEMICALS AND DISINFECTANT PREPARATIONS FOR SURGEONS' USE.

*This section has been completely rearranged. We have for some years been engaged in practically determining the Antiseptic Powers of General Chemicals as well as Proprietary Disinfectants and herein we bring our knowledge of the subject up to date.*

Of the various methods of assaying the value of a disinfectant the '**Lancet**' Method—a modification of the Rideal-Walker method—is undoubtedly the easiest to conduct and it gives satisfactory valuation.

From the historical standpoint it will be well to briefly describe the original Rideal-Walker Method:—

Rideal and Walker advocated comparison of germicidal value of different disinfectants with Carbolic Acid (c.f. B.M.J. i./c7,841).

**To conduct a Rideal-Walker determination** we operate as follows:

First prepare a standard dilution of Phenol which will kil. the test organism (*B. Typhosus*) in between 2½ and 15 minutes, e.g., strength 1 in 120. The test



consists in determining the dilution of the Disinfectant under examination that will kill the organism in the same time as the Phenol Dilution. One prepares a range of dilutions of the Disinfectant with sterile distilled water which will in all probability include the lethal strength, *e.g.* in a case in point 1 in 720, 1 in 960, 1 in 1200 and 1 in 1440. 5 Cc. of each of these are placed in a test tube rack alongside 5 Cc. of a 1 in 120 Phenol Solution. 5 drops of a 24 hours' broth growth of *B. Typhosus* are added to each tube from a pipette. Behind these 6 tubes one has 6 more racks each containing series of 5 tubes. At intervals of 30 seconds one removes with a standard platinum loop, 3mm. in diameter, loopfuls (Rideal says "five") from the front row and adds them to the tubes immediately behind. The row behind this inoculated one is then inoculated in the same way from the front row, and so on from the original until all six racks have been treated under identical conditions with exception of the time. One then incubates for 72 hours and observes the dilution, *e.g.*, 1 in 1200 in the case in point which kills the organisms (determined by the fact of opalescence of the dilution next in order) in the same time as the Phenol dilution. The R.W. Coefficient is then  $1\frac{200}{20} = 10$ . It is, of course, necessary to conduct controls throughout—broth tubes both inoculated and not inoculated.—*c.f.*, R. T. Hewlett, L.i./09,819.

It should be carefully noted that the figure for a disinfectant varies for different organisms.

In our last Edition we provided details (accumulated since 1908), of the activity of chemicals on a variety of organisms.—*B. Typhosus*, *Staphylococcus*, *B. Anthracis*. Working with all these various organisms is now deemed to complicate the issue, and we have decided to use *one organism only* in these investigations, viz., *B. Coli Communis*, as is used in the "Lancet" Method of Assay. Clearly this is, to a great extent, empirical, but only by a consummation on these lines is anything comparative attainable—in some cases, however, notes on results with other organisms are of interest and they are retained or introduced. Again certain organisms show a variable resistance to a disinfectant, *e.g.*, *B. Anthracis* and *B. Typhosus*.—*Vide* L. i./09,815.

Further we have found that some substances, *e.g.*, *Saccharin Insolubile* acts as a germicide on *B. Coli* but not as a fungicide.

The suggestion has been made to alter the Rideal-Walker Coefficient Method of examining Disinfectants by introducing organic matter—milk, urine, fæces, etc.—into the disinfectants, as it is claimed that the real test of a disinfectant is the strength and time of exposure which will enable it to kill organisms in the presence of such, but the idea has met with disfavour; and here again we fail to see how any uniform simple standardisation can be introduced with the interference of such substances.

STANDARDISATION IN PRESENCE OF FÆCES.—There is no doubt that if faecal matter be introduced as a normal standard many reputed disinfectants must lose much of their reputation.—B.M.J. i./09,286, 296.

The Garnet Method of conducting the test is described.—B.M.J.ii./09,213.

L.C.C. Report on Disinfectants:—Phenol Solution 1 in 20 and Mercuric Chloride 1 in 1,000 are true germicides for *B. tuberculosis*.—L. i./02,758.

Regulation of the Sale of Disinfectants.—Hewlett, L. i./09,893.

### **Standardisation of Disinfectants.**

Prof. Delépine emphasized the importance of distinguishing the mere inhibitory or antiseptic action from the germicidal power. His experiments show that the first product of action of Mercuric Chloride on bacteria (? Albuminate of Mercury) remains when sufficiently diluted in such a way as to prevent growth, but when the Mercury is removed, as by Ammonium Sulphide, the bacteria resume activity. Hence in all testing of disinfectants the actual death of the organisms should be ensured.

Reports on disinfectants which combine with protein or other matter or which oxidise it, must be regarded with caution when investigations have been conducted on bacteria in the absence of such organic matter (Phenols and Phenoloids are little affected by organic material of this kind). It is important to realise that the action of disinfectants is affected by protein substances, fats, urea, uric acid, organic and inorganic salts, alkalis, acids, masses of non-pathogenic bacteria, cells, etc., all of which are present in morbid products, hence it is not surprising that Prof. Delépine does not attempt to lay down conditions for tests—he regards the knowledge of the action of disinfectants as too ‘empirical.’—B.M.J. i./II, 157.

The “*Lancet*” instituted a chemical and bacteriological inquiry into the Value of Disinfectants then upon the market. The Commission appointed employed a modified Rideal-Walker method, as already mentioned, and used *B. Coli* as test organism.

**The “*Lancet*” Carbolic Acid Coefficient.** The figure representing the percentage strength of the weakest lethal dilution of the Carbolic Acid control was divided by the figure representing the percentage strength of the weakest lethal dilution of the disinfectant being tested. This was done at  $2\frac{1}{2}$  and at 30 minutes and a mean of the resulting figures was taken as the Carbolic Acid Coefficient.

The Bacteriological and Chemical results included the following:—

COAL TAR DISINFECTANTS FORMING EMULSIONS WITH WATER.—

	Co- efficients.	Phenols or Phenoloids.		Co- efficients.	Phenols or Phenoloids.
Cofectant ..	9·8	66·27	Pearson's Anti-		
Sanitas Bactox.	9·5	39·7	septic Fluid ..	2·2	20·7
„ Okol ..	8·9	48·5	Jeyes'		
Cyllin ('bulk')	8·8	40·41	(Chemists') ..	1·7	17·8
McDougall's			Lawes' ..	1·6	28·2
MOH Fluid ..	7·9	47·13	Zotal ..	1·5	10·
Kerol ..	7·7	40·56	Krysyl ..	1·3	14·16
Izal ..	7·4	41·35	Jeyes' No. 2		
Cyllin			(Grocer's) ..	0·75	5·13
Medical ..	6·4	32·08			

CLEAR WITH WATER.—

	Co- efficients.	Phenols or Phenoloids.		Co- efficients.	Phenols or Phenoloids.
Crude Carbolic			Calvert's No. 5		
Acid ..	4·2	82·65	Carbolic Acid	2·5	93·26
Trikresol ..	2·5	—	Lysol ..	1·7	50·96

L. ii./09, 1516. For a more complete abstract of this paper, vide our Edition XIV., p. 17 *et seq.*

It should be noted however that the figures for Phenols or Phenoloids were obtained by simple extraction with a solvent, the Phenol content indicated by *Bromine—the more scientific method*—was considerably less (about  $\frac{1}{2}$  in many cases).

The *Lancet* Coefficient compares % dilutions whilst the Rideal-Walker Coefficient (*c.f.* p. 186) compares the figures representing the dilutions as compared with unity—inversely.



The Commission never found such high Carbolie Coefficients as have been given by others. Many disinfectants have therefore, been incorrectly praised. Even these (bacteriological) results are not conclusive ; many other problems suggest themselves, *e.g.*, foreign substances in the matter to be disinfected, temperature, type of diluent water used, type of micro-organisms to be destroyed,—more work is required.—L.ii./09,1616.

L.ii./09,1841 replies to critics *re* the Commission report. The *Lancet* appears to justify itself on all points. It confirms that neither with the Rideal-Walker nor with the modification of the method made use of by themselves, have they under any conditions obtained (any) Carbolie Acid Coefficient figure higher than 13 amongst the disinfectants under consideration.

Sanitas Okol and Sanitas Bactox, it is contended, were examined in an old and superseded style.—L.ii./09, 1850. Sanitas Fluid should not have been classed among tar disinfectants. This was an acknowledged slip.

Full description of Sanitas,—not intended as a powerful germicide.—L.ii./09,1850.

Jeyes' Managing Director, Ainslie Walker, intimates that Jeyes' Fluid has a Rideal-Walker Coefficient ranging from 5 to 22 according to purpose required,—*e.g.*, the brands Crude Cyllin and Special Fluid Cyllin.—L.i./10,68. See also Rideal on two of Jeyes' products.—L.ii./09,1849.

Following on the " *Lancet* " Commission Report a most animated discussion on the subject took place at the Cambridge Meeting 1910, of the British Pharmaceutical Conference at which Sims Woodhead and C. Ponder (Members of the Commission) read a paper on Bacteriological Standardisation of Disinfectants. They drew attention especially to the following :—

*B. Coli Communis* as test though slightly more resistant than *B. typhosus* has the advantage of being non-pathogenic and readily recognised with great certainty by the use of McConkey's Bile-Salt Litmus Medium, *q.v.*, without the use of the microscope (change of the litmus colour by acid production).

The Number of Micro-organisms taken must be fairly large if consistent results are to be obtained, the margin of error being enormously greater where small quantities of a culture are used with a loop than when greater quantities are taken with a spoon.

The Strength and Number of Dilutions should be as close together but extend over as wide a range as possible, in order that full data may be obtained. Further, the intervals should be, as far as possible, equal, taking the form of a percentage difference. Only when these precautions are taken can the curve described be satisfactory.

The Time during which the Disinfectant is allowed to act must be more or less arbitrary, but it appears to be fair to all disinfectants (some of which act quickly and others more slowly) to take a mean between two extremes than to take any fixed point between two extremes ( $2\frac{1}{2}$  and 30 minutes).

Temperature.—A more or less arbitrary temperature being the mean temperature met with in the temperate zone, was adopted in the experiments. It has long been known that the carbolie acid coefficient of a disinfectant may vary enormously according as the work is done with solution and emulsions kept at 55° F., or maintained at a temperature of 80° F., but the authors believe that even now the great importance of the working temperature has not been realised.

Experiments conducted on a single organism give, of course, the Coefficient in respect of that organism only.—L. ii./10,418 ; P.J. ii./10,155 ; C.D. ii./10,193.

Kingzett and Woodcock supplied an elaborate paper. Coal Tar Emulsions (ready prepared), Homogeneous Coal Tar preparations (clear liquids, yielding emulsions with water) and "Chemical Germicides" (Formalin and  $H_2O_2$ ) were compared with Phenol. They modified the Rideal-Walker method to make it suitable for use with  $H_2O_2$  and Formaldehyde germicides for which, according to them, the process is not satisfactory. Ten drops of a forty-eight hours' broth culture were added to the usual amount of diluted disinfectant under examination, two loopfuls of this solution being taken according to the customary routine for sub-culture. Employing increased temperatures the "chemical" disinfectants showed a higher efficiency. It is pointed out that R.-W. Coefficients become greatly depreciated when the same preparations are examined by the Martin and Chick method (employing 3% added dried faeces), *e.g.*, two Coal Tar Emulsion Disinfectants, with R.-W. Coefficient of 22

and 18, drop to 1.6 and 1.5 by this method. Very similar drops occurred with homogeneous coal tar preparations. Added "organic matter" (not faeces) did not cause so marked a drop. They are strongly in favour of the Rideal-Walker test. The R.-W. test may very well serve to determine the relative germicidal values of similarly prepared preparations of a coal tar nature; it is not applicable for ascertaining the real or relative values of other disinfectants of a different chemical nature, nor does it, of course, afford any measure of other chemical attributes and properties possessed by them and not shared by coal tar preparations.—P.J. ii./10,157.

R. T. Hewlett in criticising Woodhead and Ponder's method thought an ordinary standard loopful should be sufficient for "seeding"; he said, the apparent necessity for the large spoon (containing 0.1 Cc.) is due to the fact that McConkey's medium is not delicate enough. Extension of time limit from 15 to 30 minutes is of questionable utility, at least for "Coal Tar" Disinfectants. A standard temperature, *e.g.*, 65° F. should always be employed. Claims that the mean between 2½ and 30 minutes raises the Coefficient over that obtained at an early period. Rideal-Walker method thought to be more stringent.—P.J. ii./10,159.

Rideal, in opening the discussion, took exception to the factor  $\frac{P-B}{3}$  (*c.f.* Edn. xiv., p. 18 for details of this) as in the case of Phenol the quotient would be zero. He said nothing definite is known about the relation between Br. absorption and germicidal action. Also discussed technique (size of spoon, etc.). Purvis pointed out the formula is purely tentative. F. J. Tocher said taking the mean of the 2½ and 30 minute results is not statistically sound. The accurate method of interpreting the results would be to evaluate the coefficient for each dilution, for each time period and to calculate the mean value of the coefficients so found. The figure obtained would give the true bactericidal measure of the disinfectant compared with Phenol under conditions of the experiment.

Sims Woodhead, in reply, contended that in his method the margin of error is reduced. Protested against being asked to accept a test because it had been the conventional standard for a number of years. The difference between the use of *B. Coli* and *B. Typhosus* is not so great as to interfere with the general run of the test.

Modification of the "Lancet" Method. A 24 hour culture of *B. Coli* is used; the experiments are always carried out at a temperature of 20° C.; the proportion of culture to disinfectant is 0.1 Cc. of culture to 5 Cc. of disinfectant; the amount of inoculation into subculture tubes is measured by loops instead of by spoons; the medium for subculture is prepared from beef extract according to the American standard and has a reaction of +1.5, the titration being carried to a point where the pink colour is distinctly perceptible. Instead of the wheel a block containing four or six grooves is used. Other minor details are given including a table of dilutions. Great variation in results may be obtained with Rideal-Walker method—it is not a method to advise for the examination of disinfectants.—Journal of Infectious Diseases, Jan., 1911, per leader in "Lancet," i./11,43.

Marchant describes a further modification of technique in the Lancet method making for greater simplicity. He proposes to substitute a modified separating flask to hold each of the mixtures of culture and graded disinfectant solution. At the necessary interval a drop from each of the mixtures can be allowed to pass into the tubes of subculture medium.—L. ii./11,1267,1282.

Anderson and McClintic use a graduated pipette for measuring the amount of test culture and adopt 15 minutes as the longer contact period in place of the 30 minutes of the "Lancet" Commission.—Proposed STANDARDISED INTERNATIONAL TEST FOR DISINFECTANTS, S. Rideal, L. ii./13,826. See also P.J. ii./12,387.

### Comparison of "Lancet" with "Rideal-Walker" Results.

In preparing our 15th Edition, we conducted experiments with a view to making a comparison between the figures given respectively by the R.-W. and the Lancet methods.

Starting with the view that the R.-W. method if correctly conducted gives results *slightly higher than the Lancet method, c.g., in*



proportion of about 9 or 10 to 7, which we believe is accepted by some workers, we found on operating with a well-known Cresylic disinfectant (Lancet figure 5·8) that we obtained the R.-W. figure of 8.

On the other hand, another Cresylic Disinfectant gave by the 'Lancet' 4·8 and by R.-W. method 14—! We think therefore the 'R. W.' method—in general may give exaggerated figures—we are strongly in favour of the 'Lancet' method in preference.

Of the organisms *B. Coli*, *B. Paratyphosus*, *Staphylococci*, *Streptococci*, and *B. Diphtheriae*, the first two were roughly far more resistant to Lysol and a series of Naphthol compounds than the others.—Zeit. f. Hygiene, Oct. 28, 1909, per M.A., 1911, p. 28.

Experiments to determine how rapidly antiseptics pass through animal membrane as estimated by destruction of bacteria. The membranes employed were celloidin and the omentum, mesentery, diaphragm and skin of the rabbit. Carbolic Acid and Mercuric Chloride were without action in 24 hours. There was, however, one exception, *i.e.*, a 5% Aqueous Phenol Solution was found to pass through the diaphragm of a rabbit in five minutes.

The most effective proved to be Iodine and Alcohol.—L. i./11, 1366.

Phenol apparently has a selective action on bacteria in sewage filters—very few types appear in the filtrate—more especially *B. liquefaciens fluorescens* and a chromogenic. Experiments showed that the liquefying organism had no action or only a slight one on the Phenol in proportion 8·4 to 16·5 per 100,000 of water, even after a month or more. When the chromogenic organism was added the Phenol content was decreased, disappearing completely in a few days. The Phenol is thought to be oxidised by the bacteria.—Na., Nov. 24/10.

Experiments using Petri Dishes of Nutrient Agar containing pieces of metal inoculated with *B. fluorescens* showed that metals produced a kind of death zone around them—this sterile zone varies with different metals. Strong action in this way was shown by thallium, cobalt, silver, mercury, antimony, and arsenic. Slight power on the other hand was seen in the case of bismuth, lead, nickel, iron, aluminium, zinc, and copper.—L. i./11, 1373.

G. T. Morgan and E. A. Cooper determined the influence of the chemical constitution of certain organic Hydroxyl and Aminic Derivatives on their germicidal power by a somewhat modified Carbolic Coefficient Method, using *B. Typhosus*, *Staphylococcus Pyogenes Aurcus* and *B. Coli*. The germicidal power of the alcohols is far less than that of the phenols, the primary alcohols being more active than the secondary and tertiary alcohols. The carbolic-acid coefficients of the cresols and *m* and *p* nitrophenols are greater than unity, and two of the isomeric dihydroxynaphthalenes ( $\beta\beta = 2:3$  and  $2:7$ ) are very active in aqueous solution, although the dihydroxybenzenes do not show any exceptional bactericidal power. The germicidal action of the aromatic amines is very low and stands in marked contrast to that of the aliphatic amines which, with the exception of the ethylenediamine, gave high coefficients, the number for *n*-heptylamine being 24·3. The hydrogenation of an aromatic amine raises the coefficient, *ac*-tetrahydro- $\beta$ -nephthylamine giving the value 5·3. The lowest coefficient (·18) for any base was given by pyridine.—C.D. ii./12.

Coal Tar Disinfectants examined as to toxicity by infection of mice, determining thereby the least fatal dose comparing with Phenol. The same relation probably exists for man. Many labelled non-poisonous are toxic to mice.—Worth Hale, Bull. No. 88, Hyg. Lab. Washington, D.C.—L. ii./13, 1204.

So far it will be seen we have mainly dealt with various Proprietary (mostly Cresylic) Disinfectants. We have quite recently (1914) operated on a number of recognised antiseptic bodies and have incorporated our results in the following pages. We also took into consideration a number of substances not hitherto examined—which might have antiseptic power—these are also indicated.

Somewhat curiously amongst the *relatively potent* are **Thorium Nitrate, Acetic Acid, Acid Citric, Acid Lactic, Acid Picric, Alcohol 70%** (the last mentioned being in confirmation of existing knowledge), **Potassium Chlorate, Saccharin Insoluble**, whilst on the other hand the *impotency* to kill disease organisms of the following chemicals:—**Antimony, Potassium Tartrate, Arsenious and Arsenic Oxide, Arsamin, and Acetone** is of interest.

*All the results have been obtained by procedure strictly in accordance with the "Lancet" Method* For practical purposes an exact determination of the *Coefficient* is not necessary. *All that the practitioner wants to know is, whether a specific disinfectant will kill the organism in a reasonable time—if in the prescribed 2½ minutes so much the better*—this we have stated also in many cases a figure for the result of 30 minutes contact.

In our last Edition we gave several factors which go to make an Ideal Disinfectant. For these Prof. Hewlett's Lectures "The Ideals for a Disinfectant," L. i./09,741,815,889, may well be consulted. Clearly we must have high germicidal power, and it must not be affected markedly by heat. The disinfectant should have no corrosive action on metals; it must be miscible or form a fine emulsion with water and so on.

In the first of these lectures a useful hint occurs as to the use of a torch flame generated by a cyclone burner burning paraffin, similar to that used on night works, &c., for disinfecting walls, floors, &c.

#### Disinfection, Mechanism of.

Formaldehyde, Halogens, Mercuric Chloride, Acids and Alkalis form chemical combinations with Proteins. Action of Phenols and Cresols in regard to Proteins is not understood. Alcohol depreciates whilst Hydrochloric Acid increases effect of Phenol. Meta-cresol precipitates Proteins in lower concentration than Phenol hence more active. E. A. Cooper has evolved a theory that the action of Phenols on bacterial proteins is not directly bactericidal. The germicidal action which follows absorption does not seem to be the result of a typical chemical union between the Phenols and bacterial Proteins.—L. ii./12,1387. The question is raised as to affinity between Essential Oils and bacterial Protein which gives these Oils such remarkable power—we refer to this under Olea Essentialia, Antiseptic Powers of.

*It will be convenient to summarise briefly all our Experimental Results before giving details. It is clear that only the following have any practical therapeutic value from the point of view of antiseptic action, i.e., they are germicidal (to B. Coli) in the strengths indicated:—*

Acetanilidum	.	.	.	1 in 400
Acetonum	.	.	.	1 in 2
Acidum Benzoicum	.	.	.	1 in 500
„ Cresylicum	.	.	.	1 in 200
„ Oxalicum	.	.	.	1 in 200
„ Picricum	.	.	.	1 in 400



Acidum Salicylicum	-	1 in 1,000
„ Sulphuricum	.	1 in 200
<b>Alcohol</b>	-	70%
<b>Argenti Nitras</b>	-	1 in 2,000
Bromum	-	1 in 20,000
Chlorinum	-	1 in 75,000
Chloroformum	-	1 in 200
<b>Creosotum</b>	-	1 in 300
<b>Formaldehydum</b>	-	1 in 50
Hydrargyri et Zinci	-	
Cyanidum (as dusting powder)	-	
<b>Hydrargyri Iodidum</b> (as Mercuric Potassium Iodide)	-	1 in 100,000
<b>Hydrargyri Perchloridum</b>	-	1 in 100,000
<b>Hydrargyri Cyanidum</b>	-	1 in 2,500
<b>Iodum</b>	-	1 in 50,000
Potassii Chloras	-	1 in 50
<b>Potassii Permanganas</b>	-	1 in 2,000
Saccharin Insolubile	-	1 in 40
<b>Sal Alembroth</b>	-	1 in 90,000
Sodil Salicylas	-	1 in 20
<b>Thymol</b>	-	1 in 1,500
Vesalvine S.	-	1 in 20

Acetanilide. 0.25% Solution killed *B. Coli* in  $2\frac{1}{2}$  minutes; 0.125% did not.—*W.H.M., Expt., 1914.*

Acetone. 50% killed *B. Coli* in  $2\frac{1}{2}$  minutes, 40% did not.—*W.H.M., Expt., 1914.*

Acidum Aceticum. 7% kills *B. Coli* in  $2\frac{1}{2}$  minutes, 5% does not kill.—*W.H.M., Expt., 1914.*

Acidum Acetyl-Salicylicum. We have not conducted experiments on the Carbolic Acid Coefficient with this acid. The gradual hydrolysis which would occur at blood heat would vitiate the result. *R. Stockman* states: A solution of strength 1 in 250 does not stop yeast fermentation, hence any antifermentative or antibacterial action must only occur when the Salicylic Acid is split off (Salicylic Acid 1 in 2,000 inhibits fermentation entirely and 1 in 5,000 greatly delays it).—*B.M.J. i./13,598.*

Acidum Arsenicum. 1% of Arsenic Anhydride did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.

Acidum Arseniosum. 2% of Arsenious Anhydride did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—*W.H.M., Expt., 1914.*

Acidum Benzoicum. 0.2% killed *B. Coli* in  $2\frac{1}{2}$  minutes.—*W.H.M., Expt., 1914.*

Acidum Boricum. 1 in 25 (Saturated Solution) did not kill *B. Coli* in  $2\frac{1}{2}$  or 30 minutes—and did not kill *Staphylococci* or *B. Typhosus* in 2 minutes.—*W.H.M., Expt., 1914.* In no sense a disinfectant, but used in sufficient quantity it is a food preservative. The figure necessary

for milk preservation is variously stated; 1 in 500 is usually advised, *c.f.* p. 271. 4% is usually employed as douche for the eyes and vagina and as mouth-wash.

**Acidum Cacodylicum.** 10% Solution did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—*W.H.M., Expt., 1914.*

**Acidum Camphoricum.** 0.5% (Limit of Solubility) did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—*W.H.M., Expt., 1914.*

**Acidum Carbolicum** (see also "*Lancet*" and Rideal-Walker Coefficients, *antea*). 1.1% killed *B. Coli* in  $2\frac{1}{2}$  minutes; 0.7% killed in 30 minutes, not in  $2\frac{1}{2}$  minutes.

Liquid Phenol (10% water added) is caustic and anæsthetic. 1% is used as vaginal injection, mouth-wash and gargle.

Solution 1 in 20 is truly germicidal for *B. Tuberculosis*.—*L.C.C. Report, L. i./02,758.*

The activity of this disinfectant on *B. Coli* is only slightly reduced by fæces and urine.—*Hewlett, i./09,816.* Alcohol diminishes activity of Carbolic Acid. Most Carbolic soaps of commerce are useless as disinfectants.—*L. i./09,818.*

**Acidum Chromicum.**  $2\frac{1}{2}$ % killed *B. Coli* in  $2\frac{1}{2}$  minutes.—*W.H.M., Expt., 1914.* Also kills *Staphylococci*. This strength is used for ulcerated gums.

**Acidum Cinnamic.** 1 in 1,250 prevents yeast growth, but 1 in 2,000 does not.—*R. Stockman, B.M.J. i./13,599.*

**Acidum Citricum.** 8% killed *B. Coli* in  $2\frac{1}{2}$  minutes. 4% killed in 30 minutes, not in  $2\frac{1}{2}$  minutes.—*W.H.M., Expt., 1914.*

**Acidum Cresotinicum.** With 1 in 1500 Solution, ortho- and the meta-Cresotinic Acids prevented growth, while with Salicylic and para-Cresotinic Acid a few colonies developed, but growth was not nearly so abundant as in the control (sterile water). With 1 in 2000 growth was obtained in all. In the case of *B. Coli* the Cresotinic Acid was more active than Salicylic Acid.—*R. May, B.M.J. ii./09,791.*

**Acidum Cresylicum.** 0.5% killed *B. Coli* in  $2\frac{1}{2}$  minutes, 0.3% did not kill.—*W.H.M., Expt., 1914.* *C.f. ante* and *Liq. Cresolis Saponatus.*

**Acidum Formicum.** 5% Solution killed *B. Coli* in  $2\frac{1}{2}$  minutes, 2% did not.—*W.H.M., Expt., 1914.*

**Acidum Hydrochloricum.** The acidity of the gastric juice probably serves as a protection against typhoid and cholera. Experiments by the late A. Macfadyen support this view.—*Hewlett, L. i./09,743.* Boer found that from 1 in 200 to 1 in 1,350 was necessary to kill anthrax, diphtheria, glanders, typhoid and cholera organisms, indicating variable resistance of different "non-spore-bearing organisms."—*L. i./09,815.*

**Acidum Hydrocyanicum.** (2% HCN). Does not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—*W.H.M., Expt., 1914.* Fumigation of trees is practised with this acid.

**Acidum Iodicum.** 1 in 2,500 is deodorant and preservative. 1 in 500 is used as mouth wash and for ulcers.



**Acidum Lacticum.** 1% of actual Lactic Acid or less killed *B. Coli* in  $2\frac{1}{2}$  minutes.—W.H.M., Expt., 1914.

**Acidum Oxalicum.** 0.5% Solution killed *B. Coli* in  $2\frac{1}{2}$  minutes.—W.H.M., Expt., 1914. Hailer ("Chemisches Zentralblatt," 1910, I) found adding Oxalic Acid increases the disinfecting power of Phenols.

We had occasion to examine several Cresylic Disinfectants for this body without finding it.

**Acidum Picricum.** 0.25% killed *B. Coli* in  $2\frac{1}{2}$  minutes.—W.H.M. Expt., 1914.

**Acidum Pyrogallicum.** 1% did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—W.H.M., Expt., 1914. 3% according to Rideal kills most organisms.

**Acidum Salicylicum.** 0.1% kills *B. Coli* in  $2\frac{1}{2}$  minutes, 0.05% does not. (Saturated Solution is of strength 1 in 500). Must not be used to the eyes. 0.2% killed *B. Typhosus* in 2 minutes.

1 in 2,000 inhibits fermentation entirely, and 1 in 5,000 greatly delays it.—R. Stockman, B.M.J. i./13,598.

**Acidum Sulphuricum.** 0.5% Solution killed *B. Coli* in  $2\frac{1}{2}$  minutes, 0.1% did not.—W. H. M., Expt., 1914. 0.05% stated to be fatal to *B. Cholerae* after 15 minutes contact.—Rideal.

**Acidum Sulphurosum.** 1% of the Off. 5% Acid killed *Staphylococci* and *B. Typhosus* in  $2\frac{1}{2}$  minutes.—W. H. M., Expt., 1914.

Gaseous sulphurous Acid was until recently much used to disinfect rooms. The gas, however, is not powerful enough to kill *Anthrax* spores.

It was found that *B. Coli* and *S. Pyog. Aureus* were killed in 24 hours in a sealed room into which 20 ounces of  $SO_2$  were passed. *B. subtilis* spores were not killed. R. mentions that a Bisulphate and Bisulphite together would be useful as they liberate  $SO_2$  on moistening, thus:



Klein says although most pathogenic organisms do not thrive in an acid medium some putrefactive and zymogenic bacteria, e.g., *B. subtilis*, *M. ureæ*, will, e.g., in acid urine.

**Acidum Tannicum.** 2% Solution did not kill in  $2\frac{1}{2}$  minutes. 40% Solution did not inhibit fungoid growth.—W.H.M., Expt., 1914.

**Acidum Trichloraceticum.** 1 in 500 solution failed to kill *Staphylococci* and *B. Typhosus* in  $2\frac{1}{2}$  minutes. In throat affections (see Text) 1 in 1 or 1 in 2 Glycerin is astringent. 1 in 4 on a tampon with endoscope in gonorrhœa has been used. Less painful than Silver Nitrate.

**Alcohol.** 70% killed *B. Coli* in  $2\frac{1}{2}$  minutes. 35% did not.—W.H.M., Expt., 1914. It is not in itself reliable as an antiseptic.

The maximum efficacy as a disinfectant is obtained with Alcohol of 70% strength. Stronger Alcohol does not penetrate Albumin so readily and is, therefore, not so active as a germicide.

**Allyl iso-sulphocyanidum.** See *Oleum Sinapis Essentiale*.

**Allyl Sulphide.** 1 in 100 in a special Saponaceous Solution killed *B. Coli* in  $2\frac{1}{2}$  minutes. Less dilutions failed to kill. Further 1 in 500 killed in 30 minutes. C.A. Coefficient is approximately 2.

A simple Aqueous Solution cannot be used in sufficient strength.—W. H. M. by Expt., 1914.

**Aluminii Chloras** (as Mallebrein). 2½% Solution kills *B. Coli* in 30 minutes but not in 2½ minutes.—W. H. M., Expt., 1914.

**Ammonia**. 1% of Ammonia did not kill *B. Coli* in 2½ minutes.—W. H. M., 1914.

A solution of Ammonia containing 0.5 Cc. of strong solution of Ammonia in 600 Cc. of Normal Saline killed *B. typhi* and *B. cholerae* and partially *B. Coli* and *M. pyogenes aureus* in 4 hours. In the case of cholera the germicidal effect takes place in a few seconds.—Hewlett, L. i./09,743.

**Antimonii et Potassii Tartras**. 5% solution did not kill *B. Coli* in 2½ minutes.—W. H. M., 1914.

**Argenti Nitras**. 1 in 2,000 solution killed *B. Coli* in 2½ minutes.—W. H. M., 1914.

Lotions, Eye Drops, and Urethral Injections 1 in 1,000 up to 1 in 500. In eye work is more penetrating and active than the organic silver compounds on the market (see Text).

Boer found that from 1 in 4,000 to 1 in 20,000 killed anthrax, glanders, diphtheria, cholera, and typhoid organisms in 2 hours—i.e., a very variable resistance by different non-spore bearing bacteria.—L. i./09,815.

**Arsamin**. 10% solution did not kill *B. Coli* in 2½ minutes.—W. H. M., Expt., 1914.

**Arsenic**. See *Acidum Arsenicum et Arseniosum*.

**Auri Cyanidum**. 1 in 2,000,000, according to Koch, of  $\text{Au}(\text{CN})_3$  dissolved in Potassium Cyanide checks growth of *B. Tuberculosis*.

**Borates and Boric Acid**. See *Acidum Boricum*.

**Bromum** 1 in 20,000 killed *B. Coli* in 30 minutes, 1 in 8,000 in 2½ minutes.—W. H. M., 1914. Was found by Arbourg and confirmed by Koch, to be the most powerful of all destructives to Anthrax and Tubercle bacteria.

**Calcii Hydras** (Slaked Lime) is not an antiseptic of any note.

**Calcii Permanganas**. See *Potassii Permanganas*.

**Carbonis Bisulphidum**. Antiseptic, but odour and inflammability prevents its use.

**Chlorinum** 1 in 75,000 kills *B. Coli* in 2½ minutes.—W. H. M., 1914. A cold saturated solution of Chlorine Water contains 0.634% by weight.

It is satisfactory to note that 'Chlorine Gargle,' which contains about 0.125%, is a potent antiseptic against this and other organisms.

Suitable for treating drinking water. No potable water would be likely to contain more than a small fraction of the number of cholera vibrios introduced into different waters used experimentally in the investigation in question (ranging from about 1,000 to 18,000 per Cc.). It was concluded that most waters would be freed from cholera vibrios, if treated with 1 of chlorine per million for 15 minutes.—L. ii./10,1213; c.f. also Vol. I., p. 234.

**Chloroformum**. 0.5% solution kills *B. Coli* in 2½ minutes, 0.2% does not.—By Expt., W. H. M., 1914. Our experiments showed further that 0.2% did not kill *Staphylococcus*, nor *B. typhosus*.



**Chromates.** See *Acid Chromic*.

**Colloidal Solutions of Copper, Gold, Mercury, Platinum, Selenium and Silver** were tested after  $2\frac{1}{2}$  minutes, 30 minutes and 16 hours' contact with *B. Coli*. With the exception of Mercury, which killed at  $2\frac{1}{2}$  minutes, none had any disinfectant power at  $2\frac{1}{2}$  and 30 minutes. After 16 hours Silver and Gold (electrically prepared) inhibited growth. Gold (chemical), Platinum, Copper and Selenium did not inhibit growth. (Two experiments were done on all except Mercury, three experiments).—*W. H. M., Expts., 1914.*

**Rhodium Colloidal Solution** (made by a modification of Bredig's process, using Rhodium terminals under pure Distilled Water). Experiments on *B. Coli*, pneumo-, meningo-, and Staphylococci showed that it had practically no germicidal action. Non-toxic by experiments on fish, frogs, rabbits and dogs. The solution had no appreciable action on the nervous system, the kidneys or the blood circulation.—*Comptes Rend., 1911, 153, 1088.*

**Collosol Argentum** (c.f. Vol. I., p. 320), is stated to kill *B. Coli* in 10 seconds.

**Copper Salts.** See below.

**Creosote (Morson).** 1 in 350 killed *B. Coli* in  $2\frac{1}{2}$  minutes.—*W. H. M., 1914.* 1 in 150 is used in phthisis, &c., see text.

**Cupric Chloride.** Kraemer has advised for treating water 1 in 5,000. Is a stronger antiseptic than copper sulphate for the treatment of water supplies. A solution containing 1 of copper in 5,000 will kill *B. Typhosus* in slightly over an hour and *B. Coli* in an hour. (*Staphylococcus Pyogenes Aureus* is killed in less than two hours by a 1 in 7,000 copper sulphate solution.—*Journal of Sanitary Institute, Vol. XXV., 1904*).

**Cupri Sulphas.** 1% killed *B. Coli* in 30 minutes but not in  $2\frac{1}{2}$ .—*W. H. M., 1914.* 1% is used for irrigation, see Vol. I., Text.

**Ethyl Iodidum.** Readily destroys *B. Tuberculosis*. (R.).

**Fluorinum.** More active than Chlorine. Fluorides and Silicofluorides (c.f. Salufer) are antiseptic. Fluoric Acid and Ammonium, Potassium and Sodium Fluorides are used in the brewing trade. 0.3% will prevent the acidity of butter, and in a trial found not to be injurious to health. (R.).

**Formaldehyde** 2% (=5% Formalin) kills *B. Coli* in  $2\frac{1}{2}$  minutes. 1% Formaldehyde does not kill in  $2\frac{1}{2}$  minutes.—*W. H. M., by experiment, 1914,* but a small proportion inhibits growth (multiplication). Formaldehyde, it would appear, is a slowly acting germicide. Kingzett and Woodcock, for example, found recently that when heated (incubated) in the ordinary way it has a coefficient 0.38, while if allowed to act for  $1\frac{1}{4}$  hours its destructive power becomes greater than Phenol. We believe that very similar, and even more marked results would be obtained with many antiseptic bodies. 1 to 2% is suitable for wounds, hands, instruments and room disinfection. It is a valuable deodorant, 5 or 10% is sufficient.

Its use as milk preservative in Great Britain is now forbidden. For detection in Milk, v.p. 270 et seq.

10% solution is useful for disinfecting human discharges, allowing an exposure of 1 hour. Tubercle bacilli in sputum are killed by 5% solution in this time.—*L. ii./07, 1178.*

### *Fumigation of Rooms.*

Hewlett, *L. i./09, 744*, says Formaldehyde is probably more active than Sulphurous Acid in general disinfection.

Kenwood (*vide C. & D., Aug. 29, 1908*), concluded from results with fumigation by Formaldehyde in 1906, and by 1% Spray of Sublimate in 1907, that there was little to choose between the two. Washing infected rooms with soap equally important.

Formalin probably owes its antiseptic power to the ease with which it abstracts oxygen and becomes Formic Acid, a process which causes the breakdown of organic matter.—*Pharmacol. 71.*

For disinfecting books.—Formalin vapour is useless. Exposure to a temperature of 180°—190° C. in a hot air steriliser for an hour or two on three successive days is effective.—*M.A., 1911, 707.*

0.8% of Formaldehyde kills *B. Diphtheriæ* in 10 minutes, *B. Dysenteriæ* in 60 minutes, *B. Typhosus* in 40 minutes, *Staphylococcus pyogenes albus* in 60 minutes, *Staphylococcus pyogenes aureus* in 40 minutes. 2% Formaldehyde killed *Staphylococcus pyogenes albus* in 30 minutes, *B. Dysenteriæ* in 40 minutes, *Staphylococcus pyogenes aureus* and *B. Typhosus* in 20 minutes. 4% Formaldehyde killed all the non-sporing organisms investigated in less than 10 minutes except *B. Dysenteriæ* and *Staphylococcus pyogenes aureus*, which, however, were killed after 10 minutes.—*B.M.J.E. ii./08, 7.*

Guaiacol is stated to have greater bactericidal power than Phenol, i.e., as 5:2.

Glycerin is preservative for vegetable preparations (c.f. *Glyce-tracta*), but, as anticipated, our experiments gave + with pathogenic organisms.

Helmitol. 5% Solution did not kill *B. Coli* in 30 minutes.—*W. H. M. Expt., 1914.*

Hexamethylene Tetramine. 10% did not kill *B. Coli*, but a less proportion inhibits growth gradually in acid solution—hence effect in bacilluria.—*W. H. M. by expt., 1914.* (c.f. *Hexamethylene tetramine*, this volume, and *Vesalvine 'S.'*).

Hyrargyri-Ammonio Chloridum (Sal Alembroth). 1 in 90,000 killed *B. Coli* in 2½ minutes, 1 in 120,000 did not.—*W. H. M.*

Hydrargyri Cyanidum. 1 in 2,500 killed *B. Coli* in 2½ minutes, 1 in 3,000 did not.—*W. H. M., 1914.* As gargle 1 in 10,000 is used. We should prefer 1 in 5,000 at least. For fibroid rhinitis tampons impregnated with 1 in 2,500 have been employed (c.f. *Text*). It is extremely poisonous.

Hydrargyri Ethylen-diamin-sulphas. We found 1 in 1,000 failed to kill *Staphylococci*, but killed *B. Coli* and *B. Typhosus* in 2½ minutes. As vaginal douche and hand disinfectant 'non-irritant,' 1 in 2,000 to 1 in 1,000 employed (= *Sublamin*).



**Hydrargyri et Zinci Cyanidum.** We found 2 minutes with the 33% paste (q.v.) killed *Staphylococci* and *B. typhosus*. As first dressing to wounds 3% gauze and wool and paste are non-irritant.

**Hydrargyri Iodidum Rubrum** used as *Mercuric Potassium Iodide*. 1 in 100,000 killed *B. Coli* in  $2\frac{1}{2}$  minutes.—W. H. M. For hands 1 in 4,000, Collyrium 1 in 5,000, wounds 1 in 7,000, vaginal douche 1 in 10,000. Not so irritant as the *Perchloride*.

**Hydrargyri Oxycyanidum.** 1 in 1,000 or more kills *B. Coli* and *B. Typhosus*. As pigment in syphilis 0.2 to 0.6%.

**Hydrargyri Perchloridum** 1 in 100,000 killed *B. Coli* in  $2\frac{1}{2}$  minutes.—W. H. M. It is the most powerful antiseptic known. Its intensity is increased by presence of *Hydrochloric Acid*, e.g., 1 in 500 with 1 in 120 of acid, for disinfecting excreta. (Woodhead says  $\frac{1}{2}$ % *Hydrochloric Acid*.) It is precipitated by soluble organic matter. For eye, nose and mouth lotion 1 in 4,500, vagina 1 in 10,000. For linen, rooms, gynecologists' hands and superficial wounds 1 in 10,000 to 1 in 1,000.

Paul and Krönig showed that of *Equimolecular Solutions* of this salt, the bromide and the cyanide, the antiseptic power (on *B. Anthracis Spores*) was in this order—corresponding to the degree of dissociation in the three solutions.—*Pharmacol*, p. 15.

RELATIVE ANTISEPTIC POWERS OF CORROSIVE SUBLIMATE AND ITS DOUBLE SALTS WITH RESPECTIVELY, AMMONIUM CHLORIDE, POTASSIUM CHLORIDE AND SODIUM CHLORIDE.

In some experiments which we conducted (January 1912) to compare the antiseptic powers of these combinations respectively with that of Sublimate in aqueous solution and equimolecular equivalents, in each case it was found that 1 in 250,000 of Sublimate either alone or so combined failed to kill *B. Coli* in 15 minutes. A 1 in 100,000 Solution in each case prevented growth of the organism. (c.f. *Researches of Koch*, Vol. I., p. 418, also *Prof. Delépine*, p. 187.)

Our test was conducted (in two separate series of experiments) by adding 5 drops of 24 hours culture of *B. Coli* to 5 Cc. of each of the solutions and after 15 minutes contact transferring a loopful of each mixture to 5 Cc. of *McConkey's Bile Salt medium* and incubating 24 hours at 37° C.

It is evident, therefore, that the formation of the double salts in question has no particular effect on the antiseptic power of Sublimate. It is probable, however, that a relatively larger proportion of one or other of the salts might have the effect. A further investigation of the relative antiseptic powers on these lines would be of interest, especially if simultaneously the astringent properties on cut surfaces were taken into consideration.—W. H. M.

Bactericidal action of pure *Mercury Oxycyanide* and a sample containing much Cyanide found to be equal against *B. Coli*, *Staphylococcus Pyogenes*, etc. Sodium Chloride enhanced bactericidal action by increasing absorption by the protoplasm of the germicide organism. Paul and Krönig's statements may be taken as a guide, but biological relations must be fully considered before a general rule is formulated.—P. J. ii./13,607.

A little Hydrogen Sulphide should be added to subcultures in testing power of this substance to prevent the sublimate carried over with the bacteria from interfering with results.—*L. i.* /09,815.

Sodium Chloride reduces power on anthrax spores.—*L. i.* /09,818.

Hydrogenii Peroxidum (10 Vol.). 12% did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—*W. H. M.*, 1914. Is variously employed: even the strong official solution may be employed on mucous membrane. It is used in the Budde process of sterilising milk (*q.v.*) and is contained in *Sanitas q.v.*

Hyperol. 2% kills *B. Coli*.—*P. J. i.* /14,363.

Iodine. 1 in 50,000 kills *B. Coli* in  $2\frac{1}{2}$  minutes.—*W. H. M.*, 1914. It is much employed as a first aid dressing and to sterilise catgut (*q.v.*). Iodine is potent against other organisms, but unfortunately, to check *B. Anthracis* once established in the human body 12 Gm. of Iodine would have to be in constant circulation in the system. (*Koch.*)

Iodoform. A paste of Iodoform will kill *B. Coli* and *B. Typhosus* in  $2\frac{1}{2}$  minutes, but not *Staphylococci* invariably. Is used as a bladder injection with glycerin, also as a dusting powder and wool dressing.

If Iodoform be dusted on to sterile nutrient plates growth takes place from organisms contained in the Iodoform. A "50% Solution" (? how made) will hardly kill *Staphylococci*. It is said to be toxic producing various symptoms.—*L. i.* /13,1245; *L. i.* /13,1346. In answer to this it is said that even Corrosive Sublimate (dry) will contain micro-organisms.

Iron. Frankland proved that Metallic Iron is destructive to bacteria. Ferrous Sulphate is stated to be mildly antiseptic. Ferric Sulphate and Chloride check fermentation and bacterial growth.

Lead Salts. Are antiseptic. 2.0 Gm. per litre are stated to preserve broth. We have not experimented with these.

Liquor Aluminii Acetatis *P. G.* kills *B. Coli* in 30 minutes but not in  $2\frac{1}{2}$  minutes.—*W. H. M. Expt.*, 1914.

Liquor Carbonis Detergens. We found a 2% solution killed *B. Coli*, *B. Typhosus* and *B. Anthracis* in  $2\frac{1}{2}$  minutes. A remedy in skin affections, strength used 1 in 8 up to 1 in 160 (see Text).

Liquor Cresolis Saponatus, *U.S.* 0.5% killed *B. Coli* in  $2\frac{1}{2}$  minutes.—*W. H. M. Expt.*, 1914. *C.A.* Coefficient 1.5. For midwifery 1% is usually employed.

Lister's Antiseptic. See Hydrargyri et Zinci Cyanidum.

\*Lysoform. 2% kills *Staphylococci* and *B. Anthracis*, but at least 10% is necessary for *B. Coli* and *B. Typhosus*.—*W. H. M. Expt.*, 1912.

It is employed for wounds and irrigation. Contains Formaldehyde. Lathers with water. Non-poisonous. For further details *v.* Vol. I., p. 115.

Magnesii Sulphas. 20% solution did not kill *B. Coli* in 30 minutes.—*W. H. M.*, 1914.

Mallebrein. See Aluminii Chloras.

Malourea, *Syn. Veronal*. 1% (at 37° C.) failed to kill *B. Coli* in 30 minutes.—*W. H. M.*, *Expt.*, 1914.

Mercuric Chloride. See Hydrargyri Chloridum.



**Mercuric Cyanide.** See *Hydrargyri Cyanidum*.

**Naphthalene.** A paste we found will kill *B. Typhosus* but not invariably *Slaphylococci*.

**Enemala** of 8 grains have been used. Parasitic in scabies, 10 to 20% solution in oil. Is commonly employed as deodorant in closets, but not a disinfectant in this way.

**Naphthol  $\beta$ .** A paste we found will kill *B. Typhosus* and *Slaphylococci*.

**Oily Solution** 10% has been used. This appears to be active.

**Nicotinæ Tartras.** 10% solution kills *B. Coli* in 30 minutes, but not in  $2\frac{1}{2}$  minutes.

**Oleum Allii.** See *Allyl Sulphide*.

**Oleum Sinapis Essentiale.** 0.1% did not kill *B. Coli* in 30 minutes.—*W. H. M. Expt.*, 1914.

**Oils Essential.** See Vol. I., pp. 549, 550, Vol. II., p. 101 et seq.

**Oxygen** in the nascent condition, e.g., from *Polassium Permanganale*, is antiseptic.

**Ozone** in the dry state has little action on micro-organisms.

**\*Paraform.** Using a paste with water we found to kill *Slaphylococci* and *B. Typhosus* in 2 minutes. The spontaneous vapour (*Formaldehyde*) has been used to maintain instruments and catheters in sterile condition. For fumigation of rooms during and after disease. Tablets (15 grains) are made. 20 of these disinfect 1,000 cubic feet space.

**Persulphates** are Antiseptic. **Ammonium Persulphate.** 1 to 2% kills *Cholera* organisms and others in a few minutes.

**Sodium Persulphate.** 2% solution did not kill *B. Coli* in 30 minutes.—*W. H. M., Expt.*, 1914.

**Phenazonum.** 10% solution did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—*W. H. M. Expt.*, 1914.

**Phenoloid Disinfectant.** Lancel Carbolic Coefficient 7.8, v. Vol. I. p. 37.

**Potassii Bromidum.** 20% did not kill *B. Coli* in 30 minutes.—*W. H. M. Expt.*, 1914.

**Potassii Chloras.** 2% kills *B. Coli* in  $2\frac{1}{2}$  minutes; 1% kills *B. Coli* in 30 minutes, but not in  $2\frac{1}{2}$  minutes.—*W. H. M. Expt.*, 1914.

**Potassii Permanganas.** 1 in 2,000 kills *B. Coli* in  $2\frac{1}{2}$  minutes; 1 in 5,000 does not, but does so in 30 minutes. A previous experiment showed C.A. Coefficient 90.—*W. H. M.*, 1914. It is a good deodorant.—*Rideal*. In presence of organic matter, however, its antiseptic power is reduced by it oxidising the organic material.—*B.M.J.* ii./09, 212. (*Calcium Permanganas* approximates the *Polash Salt* in potency.)

In gonorrhœa 1 in 1,000 gargle and vaginal douche 1 in 5,000 of either salt are employed. Bousfield found sewage as control in his experiments gave an average of 239 colonies in 0.00001 Ce. against sewage with 1 in 5,000 permanganale 99, 1 in 2,500 23, and 1 in 1,000 one colony—the time of contact being 12 hours. Further work showed that the time element is of no importance whatever—results after 5 minutes contact were quite as good as after 4 hours. A source of error

in the Rideal-Walker method was overcome in these tests by diluting the disinfectant after 12 hours' contact to 1 in 100,000 of the strength at which it had been allowed to act for the purposes of the experiment before making the cultures. The general conclusion was that 1 in 1,000 is efficient and that if such a mixture of permanganate and sewage is deodorised it is also sterilised.—L. ii./o8,1078.

**Pyoktanin.** 1 in 500 or even 1 in 2,000 arrests *B. typhosus* and *B. Coli*.—Rideal.

**Pyrogallol.** See Acid Pyrogallic.

**Quininæ Hydrochloridum Acidum.** 10% Solution did not kill *B. Coli* in  $2\frac{1}{2}$  minutes.—W. H. M. Expt., 1914.

**Quininæ Sulphas.** 1 in 500 Solution necessary for killing infective organisms (in a common cold).—L. ii./o8,1661. See also Quinine Sulphate, Vol. I.

**Resorcin.** 3.5% killed *B. Coli* in  $2\frac{1}{2}$  minutes, 1% did not kill in 30 minutes.—W. H. M. Expt., 1914.

Is non-irritant on mucous membrane, e.g., bladder, 5% is used. As collyrium 2%, as enema 0.5%. See also Text.

**Saccharin, Insoluble.** 0.25% killed *B. Coli* in  $2\frac{1}{2}$  minutes.

**Saccharin, Soluble.** 5% did not kill *B. Coli* in 30 minutes.—W. H. M. Expt., 1914.

**Sal Alembroth.** See Hydrargyri-Ammonio Chloridum.

**Soap.** Though not giving a high Carbohc coefficient is generally acknowledged to be germicidal. We tried a 2% solution which was useless on *B. Coli*, *B. Typhosus* and *Staphylococci*, but this does not simulate the process of scrubbing or washing. c.f. for further details, p. 125.

**Sodii Chloridum.** 33% Solution did not kill *B. Coli* in 30 minutes.—W. H. M. Expt., 1914.

**Sodii Metabisulphis.** 2.5% in Glycerin kills *Staphylococci*, but did not kill *B. Typhosus* in  $2\frac{1}{2}$  minutes.—W. H. M. Expt., 1914. A pigment this strength has been used for thrush.

**Sodii Persulphas.** See Persulphates.

**Sodii Salicylas.** 5% killed *B. Coli* in  $2\frac{1}{2}$  minutes, 1% did not.—W. H. M. Expt., 1914.

A feeble germicide and anti-fermentative. It has almost no action on yeast or bacteria.—R. Stockman, B. M. J. i./13,598. See also Water Examination for *B. Coli*.

**Sodii Sulphas Acidus.** For water sterilising see Text (Vol. I.). One Antityphoid Tablet to the pint of water is stated to destroy *B. Typhosus* and *B. enteritidis* in 15 minutes. We found it killed *B. Typhosus* and *Staphylococci* in 2 minutes, in above proportion.

**Sodii Sulphis.** 1 in 500 we found did not kill *Staphylococci* or *B. Typhosus*.

**Sodii Taurocholas.** 20% solution did not kill *B. Coli* in 30 minutes.—W. H. M. Expt. 1914.

**Strychninæ Hydrochloridum.** 2.5% solution did not kill *B. Coli* in 30 minutes.—W. H. M. Expt., 1914.

\***Sublamin.** See Hydrargyri Ethylen-Diamine-Sulphas.



**Sulphonal.** 1 in 450 (saturated solution) did not kill *B. Coli* in 30 minutes.

**Tar.** See *Liquor Carbonis*.

**Terpin Hydrate.** 0.25% said to arrest *Tubercle Bacilli*. We have not experimented with this.

**Thorii Nitras.** 1% killed *B. Coli* in  $2\frac{1}{2}$  minutes.—W. H. M., 1914.

**Thymol.** 1 in 1,500 killed *B. Coli* in  $2\frac{1}{2}$  minutes, 1 in 3,000 kills in 30 minutes but not in  $2\frac{1}{2}$  minutes.—C. A. Coefficient 19 approximately.—W. H. M., 1914.

1 in 800 is used as gargle. It is soluble 1 in 1,500 water and 1 in 200 glycerin.

Ratimoff places Thymol amongst the 4 highest Antiseptics.—L. i./13,368.

**Thymol Disinfectant.** A potent germicide. *Lancet C.A.* Coefficient 10.4. Vide Vol. I., p. 771.

**Toluol** (c.f. Benzol, Vol. I., which it resembles). Did not hinder growth of *Staphylococci*.

**Trikesol.** C.A. Coefficient 2.5. 1 in 2,000 appeared to hinder *Staphylococci* and *B. Typhosus* which ultimately developed (in 60 hours).  $\frac{1}{2}$ % on the other hand, killed *B. Coli* and *B. Typhosus* but not *Staphylococci*. In general surgery  $\frac{1}{2}$  to 1%. Eye wash 1 in 1,000 to 1 in 2,000.

**Uranii Nitras.** 5% killed *B. Coli* in 30 minutes but not in  $2\frac{1}{2}$  minutes.—W. H. M. Expt., 1914.

**Veronal**, see *Malourea*.

**Vesalvine 'S.'** 5% killed *B. Coli* in  $2\frac{1}{2}$  minutes.  $2\frac{1}{2}$ % killed *B. Coli* in 30 minutes but not in  $2\frac{1}{2}$  minutes.—W. H. M. Expt., 1914.

Zinc shaken with water stated to kill *B. Typhosus* and *B. Coli communis* in a few hours. Copper has a similar effect. (Kraemer.)

**Zinci Chloridum.** The results of our tests showed that Zinc Chloride was not of much avail. 1 in 1,000 failed to kill *B. Typhosus* and *Staphylococci* in  $2\frac{1}{2}$  minutes. 1 in 500 is an astringent lotion. It is very poisonous. A  $2\frac{1}{2}$ % Solution was found to destroy bacteria, but Koch found even 5% would not kill *Anthrax* spores.

**Zinci Permanganas.** 1 in 5,000 prevented growth of *B. Typhosus* and *Staphylococci*. Employed similarly to the Potash Salt. Absence of irritation is a feature.

**Zinci Sulphanilas.** 1% killed *Staphylococci* but did not kill *B. Coli* or *B. Typhosus*. 1 in 250 killed *Staphylococci* but not the others.

**Zinci Sulphas.** 2% killed *B. Coli* in 30 minutes but not in  $2\frac{1}{2}$  minutes.—W. H. M. Expt., 1914.

**Zinci Sulphocarbolas.**  $2\frac{1}{2}$ % killed *B. Coli* in  $2\frac{1}{2}$  minutes, 1.25% did not.—W. H. M. Expt., 1914.

These results form an interesting Table vide Vol. I., p. 965.

See also *Antiseptic Powers of Essential Oils antea*.

**Sunlight** according to Koch will kill the *Tubercle Bacillus* in from a few minutes to 5 or 7 days, according to the thickness of the medium.

*Light, in short, is one of the most important agencies for diminishing the number of bacteria.*

*B. Typhosus is killed rapidly by sunlight. 240,000 organisms in 2 hours were reduced to nil (in India).—L. i./09,742.*

*Heat owes its bactericidal power to its coagulating effect on bacterial proteins. Moist heat is best because apart from its penetrating power it is well-known the protein in the dry condition coagulates at a much higher temperature than when moist.—Hewlett, L. i./09,815.*

*Filters. The 'Pasteur-Chamberland' or 'Berkfeld,' or similar apparatus of the porous candle type are efficient instruments.*

## ANALYTICAL MEMORANDA.

### I.—CHEMICAL TESTS & MICROSCOPIC METHODS FOR THE EXAMINATION OF URINE, BLOOD, FÆCES, &c.

The **Specific Gravity** of Urine (at 60° F.) is usually between 1·015 to 1·025. The volume passed per diem (24 hours) in health is about 50 ounces (1·500 Cc.). The capacity of the bladder is, as an average, 20 ounces (600 Cc.).

It is pointed out that temperature makes a considerable difference in taking the Sp. Gr., *e.g.*, a urine Sp. Gr. 1·015 when passed may be 1·020 when cooled to room temperature. The specific gravity increases about one point for every fall of 8° F. of temperature.—L. i./07,252.

In women the Sp. Gr. frequently ranges higher than in men. 1·035 to 1·040 is not at all uncommon even in health and not entirely accounted for by small consumption of liquid.—B.M.J. ii./09,652.

#### Acetone and Allied Bodies in Urine.

##### Legal's Test:—

*Fresh concentrated Sodium Nitroprusside* [ $\text{Na}_4\text{Fe}_2(\text{CN})_{10}(\text{NO}_2 + 4\text{H}_2\text{O} = 595\cdot864 \text{ I. Wts.}]$  **Solution** (soluble 1 in  $2\frac{1}{2}$ ) added to a specimen or its distillate containing Acetone, made slightly alkaline with caustic potash, produces a red colour which changes rapidly to yellow. On adding Acetic Acid a reddish-violet colour is produced, which changes to blue on standing.

**Rothera's Test** is usually given as follows:—The liquid to be tested is saturated with Ammonium Chloride. A few drops of 5% solution of Sodium Nitroprusside are added and then 1 to 2 Cc. of Ammonia Solution. In half an hour a red colour is produced. The test is sensitive to 1 part in 20,000.

One may also proceed thus—Add a little Ammonia so that it remains on top as a clear solution with the nitroprusside and urine below. If acetone is present in 1 to 3 minutes a well marked ring of magenta (petunia) appears at the juncture of the liquids and spreads upwards. An orange red ring is to be distinguished from the acetone ring.—L. i./07,805.

**"Endolytic Tubes"** (*c.f.* p. 212) are made containing Sodium Nitroprusside and Ammonium Chloride to be used in conjunction with a little washing Soda or Liquor Potassæ.

Large uses 15 Cc. Urine,  $\frac{1}{2}$  to 1 Cc. of Glacial Acetic Acid, a drop of freshly made Nitroprusside Solution and 1 Cc. of strong Ammonia Solution by which  $\frac{1}{4000}\%$  can be detected.—Cambridge, L. i./07,911.

Acetone having a specific gravity of 0·8 will obviously decrease the specific gravity of a urine, and may lead to error if its presence be unsuspected in diabetic urine. This is apt to occur in an advanced stage of the disease.



Acetonuria in cases of gastric ulcer.—L. i./03,1230.

May be associated with the administration of chloroform.—L. ii./05,583.

**Iodoform Test.** Distil the sample and make distillate alkaline with potash, add a little iodine solution (not an alcoholic solution). The formation of iodoform, recognised by yellow turbidity and the odour, indicates presence of acetone.

Examine the Iodoform crystals microscopically; the test by the smell is not entirely satisfactory.—L. i./07,805.

**Aceto-Acetic Acid.** *Syn.* DIACETIC ACID,  $\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{COOH} = 102.048$  I. Wts.

**Gerhardt's Test for.** Ferric Chloride gives red colouration. A few drops of Potassium Citrate solution instantly remove the colour. Reacts also with Sodium Nitroprusside as above but less reliable. The acid is soluble in ether, and may be removed by it after acidifying the specimen with Sulphuric Acid. Dilute Ferric Chloride solution shaken with this ethereal solution, becomes red.

“**Endolytic Tubes**” (*c.f.* p. 212) containing Ferric Chloride Solution for testing are made.

Occurs in urine in cases of gastric ulcer.

In employing the ferric chloride test care must be taken to distinguish from colour produced by salicylic acid and compounds, *e.g.*, salicin, aspirin, diuretin, salol. Also other substances in the urine may respond.—W. H. Hurtley, L. i./13,1160. For Hurtley's new test, *v. infra*.

Boil the urine first for five minutes, then apply test. As the aceto-acetic acid is converted by so doing into acetone there is considerable reduction in colour if dependent on aceto-acetic acid but is unaltered if due to salicylic acid.—B.M.J. ii./04,114; L. i./07,511.

In diabetes the ferric chloride reaction in urine indicates by the colour produced the amount of diacetic acid present and is hence measure of the acidosis when of mild degree. The *B*-oxybutyric acid, which cannot be conveniently tested for, is roughly proportional to the aceto-acetic acid present. Coma is always accompanied by a deep reaction of the urine with ferric chloride. The appearance of the reaction indicates that a benign case of diabetes has become a severe one, and that the tissue metabolism has become profoundly altered. It is important to keep a close watch on this test, both as to its presence or absence, and also as to the depth of colour obtained. In early stages patient may be still amenable to treatment. A direct change to a strict carbohydrate free diet is unnecessary and dangerous as it often gives rise to a ferric chloride reaction when none is present or increases one already existing. Gradual reduction is just as efficacious.—L. i./10,1002.

**Hurtley's Test for Aceto-Acetic Acid.**

To 10 Cc. of urine add 2.5 Cc. of Concentrated Hydrochloric Acid and 1 Cc. 1% Sodium Nitrite. Shake and allow to stand two minutes. Add 15 Cc. of strong Ammonia followed by 5 Cc. of 10% Ferrous Sulphate or a solution of Ferrous Chloride of equivalent strength (2 Gm. Fe in 100 Cc.). Shake and pour into a 50 Cc. Nessler glass. Do not filter. Violet colour forms slowly.

*Acetone does not respond to the test.*—It is exceedingly delicate. It is assumed that iso-nitroso-acetone is first formed which then colours with the ferrous sulphate.

The test can be rendered quantitative colorimetrically. The highest amount of Aceto-acetic acid found was 0.4%.—L. i./13,1160.

**Arnold's Test** is useful. Two Solutions are required (a) 1 Gm. Para-amino-acetophenone dissolved in a little water with aid of 2 Cc. of Hydrochloric Acid and the solution made up to 100 Cc. (b) Sodium Nitrite 1%. Mix 2 volumes of (a) and 1 volume of (b), add an equal volume of urine and a drop or two of strong Ammonia. Reddish precipitate forms. To a portion of this a large excess of

Hydrochloric Acid is added (1.5 Cc. to 2 Cc.)—a fine purple is formed. It is best to filter the urine through animal charcoal first—more urine can be used by so doing.—L. i./13,1160.

**Iodine Absorption Test, Bela and Ondrovich.**—5 drops of Acetic Acid 50% are added to 5 Cc. of Urine, then 1 drop of 1 in 500 Methylene Blue or *q.s.*, to give blue tint. Then titrate with N/10 Iodine Solution until a red tint appears.

$2\text{I}=\text{CH}_3\text{CO}.\text{CH}_2\text{COOH}$ . *Vide* L. i./13,1160.

Acetone bodies in the urine and clinical significance. J. E. Piper found diabetic urines, when fresh, contained 70% or more of the Acetone as Diacetic Acid. To estimate Acetone by a rough comparison of the colour produced with Sodium Nitroprusside is out of the question, because the reagent reacts with Diacetic Acid. The ROTHERA TEST (*antea*) is superior to all others.—L. ii./13,535.

The MESSINGER-HUPPERT METHOD is also employed. It consists in adding to a distillate an excess of Standard Solution of Iodine (alkaline) and titrating the amount unconverted into Iodoform.—Dixon Mann, *Physiology and Pathology of Urine*, 2nd Edition, p. 124.

**Iodic Acid, Test for.**—Add to 1 or 2 Cc. of normal urine 2 Cc. of 10% Iodic Acid Solution and 3 Cc. Chloroform. Uric Acid, etc., reduce the Iodic Acid—the Chloroform becoming coloured with the Iodine. Now add a little of the specimen to be tested and shake thoroughly. If Aceto-Acetic Acid present the colour disappears, if absent it is intensified.—M. 1906.

**Hydroxy- or  $\beta$ -Oxy-Butyric Acid**  $\text{CH}_3.\text{CHOH}.\text{CH}_2\text{COOH}=104.064$  I. Wts., and any increase in the amount of fat (lipæmia—granules stained by Osmic Acid), should be carefully looked for in the urine and blood respectively of diabetics. It may be extracted from the specimen with ether, and gives a reddish-violet colour with Ferric Chloride *vide* above—the diacetic acid gives approximate index of this acid. Occurs only if Diacetic Acid be also present, *c.f.*—B.M.J.E. i./06,49. The specimen may be fermented to remove sugar, precipitated with lead acetate and ammonia; if the filtrate be lævorotatory  $\beta$ -Oxy-Butyric Acid is probably present.—B.M.J. i./03,1205.

In diabetes, Acetone, Diacetic Acid and  $\beta$ -Oxy-Butyric Acid are excreted in this order as the disease advances, and if metabolism can be improved they disappear in the inverse order. The main source of Acetone is the imperfect metabolism of fat, either of food or the body.—B.M.J.E. ii./06,49. *c.f.* p. 207 *et seq.*

In some of the gravest forms of renal disease albumin may be absent from the urine, at any rate temporarily. An address on diagnosis of certain forms of renal disease.—B.M.J. i./07,725. Conversely serious renal disease should not be diagnosed merely by finding blood or albumin in the urine.

In following the progress of a case it is of importance to examine the mixed urine of a whole day, because if, *e.g.*, the percentage in a specimen examined were to suddenly show a rise, the quantity excreted per diem might be the same if the amount of urine, had decreased owing to the consumption of less liquid, or change of diet, occupation, &c., and *vice versa*. The same remark, of course, applies to all pathological constituents in the urine.

With regard to the various views as to reasons for appearance of  $\beta$ Oxy-Butyric Acid, Diacetic Acid and Acetone in the Urine, Mann says the tendency at the present time is to consider them as products which are found during the splitting up of fat in the tissues generally,—according to some authorities in the muscles and large glands particularly, such as the liver.

Occurrence of acetonuria in infectious diseases. By Acetone bodies are meant  $\beta$ -Oxybutyric and Diacetic Acids and Acetone. Acetone occurs much more constantly in diphtheria and scarlet fever than in enteric, of 96 cases of diphtheria 87 were found to have acetonuria and of 197 cases of scarlet fever 167 showed its presence also.—L. i./10,1346.

### Acidosis—B.M.A. DISCUSSION.

It is known that the organism normally meets the presence of Acids in the system by using an available alkali that is not essential for other purposes, namely Ammonia. Those animals that have from



their food considerable Ammonia available have the greatest power of withstanding Acid intoxication and *vice versa*. As a consequence Ammonia is excreted in abnormally large amounts in the urine and the presence of Ammonia in same in abnormal amounts becomes an index of the acid intoxication. In human beings similar circumstances maintain in certain pathological conditions.  $\beta$ -Oxybutyric Acid is the only acid known to occur in the body in amounts sufficient in themselves to be dangerous from the effects as Acid. Acetone and Diacetic Acid are oxidation products of this acid. Diacetic Acid is not directly toxic. Acetone probably occurs only in very small amounts,—it may have but a small direct share in any severe toxæmia, but it may perhaps damage the kidneys, thus tending to add renal insufficiency to the pre-existing toxæmia. The administration of alkalis often does good.  $\beta$ -Oxybutyric Acid has a large share in producing the intoxication that occurs in diabetes, but Acid intoxication does not wholly explain the conditions. Acidosis relatively slight is also seen in starvation. Various poisonings, especially some of the narcotics, in digestive disturbances, in cyclic and periodic vomiting, in acute yellow atrophy and phosphorus poisoning, in eclampsia and vomiting of pregnancy. The occurrence in diabetes is known to be dependent on inability to use Carbohydrates, and coincident excessive uses of fats. In starvation large amounts of body fat are burned.

The Author suggests the possibility that the attack of the Organic Acids may in more or less extent be upon the lipoids of the nervous system and resemble that of narcotics, others show that the acids may act in part as narcotics through the influence of the undissociated molecules upon the lipoids. With regard to the manner in which  $\beta$ -Oxybutyric Acid accumulates rather than Diacetic Acid or Acetone, it appears that a definite equilibrium is maintained between the two acids. Probably normally the oxidation does not go over to Diacetic Acid.

Various substances have been suggested to control acidosis,—*Alcohol has proved of most value*. Lately Woodyat has found that Glyceric Aldehyde largely reduces acidosis,—it is probably a normal combustion product of sugar. The best control must for the present be to gradually train the Carbohydrate metabolism back to the point where it can utilise more Carbohydrate and thus do away with the acid intoxication.—D. L. Edsall, B.M.J. ii./10,1033.

In the discussion on this paper the dietetic treatment of diabetes was dwelt on. A diabetic may be able to metabolise lævulose, oat-meal or potato starch when unable to assimilate other Carbohydrates. In other forms of acidosis dextrose is given,—if necessary per rectum. The subject of acidosis in delayed Chloroform poisoning is also discussed.—B.M.J. ii./10,1036, *et seq.*

The presence of acetonæmia in diabetes is caused by Aceto-acetic Acid decomposing. This in turn is formed from  $\beta$ -Oxybutyric Acid,—in grave cases 30, 50, or even 70 Gm. of this acid may be excreted in the course of 24 hours. A diabetic may die with some of the symptoms usually associated with coma, although he has little

$\beta$ -Oxybutyric Acid in his blood, but it is generally accepted that the characteristic air, hunger and coma, which follow upon it, are actually due to acidosis.—A. E. Garrod. B.M.J. i./11,1416.

Phthisis and diabetes frequently occur in the same family. The former is decreasing, the latter is on the increase. Is it due to open air treatment with its forced appetite? Are we trying to strengthen relatives of phthisical patients and over-straining their powers of metabolism? Is there any significance in the appearance of  $\beta$ -Oxybutyric Acid in diabetes and the absence of sweating?—B.M.J. i./10,1006.

*To combat acidosis in diabetics with large quantities of glucose seems more scientific and more likely to give benefit than alkalis,—this tackles the condition nearer its source than attempting to neutralise an already fully neutralised series of Acids, which are probably of no more importance than some of the other known chemical abnormalities, e.g., the presence of Creatin,—which accompany this condition. The term acid intoxication applied to gastro-enteritis, delayed Chloroform poisoning, etc., is a misnomer. The amounts excreted in these conditions is small in comparison with that in diabetic coma, and are thought not able to produce symptoms.—L. ii./11,10.*

**Acidosis Index.**—A clinical measure of the quantity of Acetone bodies excreted in the urine.—T. Stuart Hart, Quarterly Jl. of Med., July, 1912, p. 419.

In every case of severe pregnancy toxæmia Acetone and Acetic Acid were detected—in several milder cases both were absent. **Rothera's Test** *v. antea* modified was used for the former. 5 Cc. of urine are shaken up with Ammonium Sulphate, *q.s.*, to saturate; 0.5 Cc. of strong Ammonia Solution is added, then 3 or 4 drops of freshly made Sodium Nitroprusside Solution. If Acetone is present purple colour is produced.—L. i./13,1366.

### Albumin Tests.

**Proteins** occurring in urine are classed by Mann as—

(a) **Serum Proteins:** *Serum albumin, Serum globulin or paraglobulin and fibrin.*

(b) **Compound proteins:** *Nucleo-albumin, Chondro-albumin, Taurochol albumin and Mucins.*

(c) **Proteolytic products:** *Albumoses.*

Secondary Albumoses excepted, all the urinary proteins are precipitated by Nitric Acid. With most, excepting Albumin, the precipitate thus formed is *soluble with heat.*

ALBUMINURIA denotes the presence in the urine of Serum Albumin accompanied by varying proportion of Globulin.

Albumin is precipitated by excess of mineral acid, but not by Acetic Acid.

**Acetic Acid with heat.** Fill a test tube about half full with filtered urine, slightly acidify with dilute acetic acid. Boil the upper portion. Albumin, if present, will precipitate in the form of a cloud which will be insoluble after cooling on further addition of acetic or nitric acids in moderate amount.

**Differential Diagnosis in cases of Albuminuria.**

*The presence of Albumin seldom matters until its amount is sufficient to respond both to the Acetic Acid and boiling test, and the Cold Nitric*



*Acid Test*,—there is no need to trouble about the other Albumin tests,—there is such a thing as too great delicacy for clinical work.

In doing the Acetic Acid and boiling test it is well to add a few drops of the Acetic Acid to the opalescence if formed, *i.e.*, after boiling unless the urine be alkaline to start with, in which case it must be rendered slightly acid before being boiled. If the cloud formed disappears it is Calcium or Magnesium Phosphate, if it dissolves with effervescence it is carbonate,—if it remains unaltered or becomes thicker (flocculent) it is Albumin.

A fallacy is with regard to Nucleo-protein,—this is precipitated by Acetic Acid, and it is possible for a cloud of Phosphates to be cleared up by the latter, and yet for a faint cloud of nucleo-protein to come down in the place of the phosphates in such a way as to suggest that the original cloud was not wholly soluble in the acid, and therefore that albumin is present when it is not. There are three ways of obviating this source of fallacy; the *first* is to add a single drop of dilute nitric acid to the suspicious cloud that remains after the addition of acetic acid; if it is due to albumin, it will persist or even increase, whilst if it is due to nucleo-protein the nitric acid will disperse it; the *second* is to perform the cold nitric acid test for albumin as described subsequently—nucleo-protein will not give a definite localised white ring with it; and *thirdly*, a control test may be done, acetic acid being added to another specimen of the urine without boiling, and the cloud due to any nucleo-protein present compared with the cloud in the acidulated and boiled specimen.—Herbert French, B.M.J. i./11,417.

**Clinical Significance of Albuminuria.**—The amount of albumin detected at any time does not measure the importance of the albuminuria. A large output naturally implies failure of nutrition, but a small quantity may be of equal danger. Note Sp. Gr. and color.

The finding of Casts may be of assistance, but too much importance need not be paid to presence of a few hyaline casts (especially in centrifugalised sediment). They are likely to be found, when albumin is present, in acid urine. They may be found in any of the forms of albuminuria not associated with definite renal disease, etc. Casts and albumin are often absent from the urine for considerable time in chronic interstitial nephritis. It is not safe to base a diagnosis on the non-finding of casts where serious structural renal change is suspected. Temporary albuminuria is frequently associated with athletic exercise. The sphygmograph is often of assistance in distinguishing functional from organic types of albuminuria.

A large amount of albumin without blood or pus may generally indicate chronic tubal nephritis; confirm by high Sp. Gr. microscopic examination of deposit, and appearance of patient. A small amount in a middle-aged or elderly man will probably point to chronic interstitial nephritis. In a young man a mere trace may be only the evidence of a functional albuminuria and the diagnosis must rest on negative evidence to a large extent, a most important factor being relatively high Sp. Gr. unless this has been influenced by nervousness or recent consumption of a large quantity of liquid.—N. Tirard, L, ii./o9,1062.

Albuminuria caused by toxic effects of poisonous substances, *e.g.*, lead mercury, phosphorus, cantharides, etc.—B.M.J.E. ii./o7,81.

**Various forms of albuminuria classified and described:—**  
(a) With renal tube casts. (b) With renal tube casts and with pus.  
(c) Without tube casts. Also albuminuria due to (1) febrile conditions, (2) heart failure conditions, (3) so-called 'physiological albuminuria.'—Herbert French, B.M.J. i./11,418.

Albuminuria in pregnancy, Significance of.—A marked increase in cases of post partum hæmorrhage found, not necessarily in eclampsia but in cases of albuminuria.—B.M.J. ii./12,1009. See also L. i./13,1366.

**Asaprol** (Calcium Beta-naphthol-Sulphonate) precipitates albumin, peptone, &c., from acid solution. On boiling, peptone and albumose redissolve, albumin remains.

**Riegler's Test** ("Beta-naphthalene-Sulphonic Acid") is this.—L. ii./08, 1824; B.M.J. i./09,542.

Tablets are made—4 to be dissolved in 5 Cc. of water for use.—Add to 5 Cc. of the specimen filtered if necessary.

**Carbolic Acid** (saturated solution in absolute alcohol) has been used, but is not so delicate as Salicyl-sulphonic Acid, but the latter (see below) may be too delicate for clinical work. Further, the milkiness produced by the Phenol emulsifying with the water is a drawback.—L. i./99,1393.

### **Ferrocyanic Acid Test Pellets.**

Potassium Ferrocyanide,  $K_4Fe(CN)_6 + 3H_2O = 422.358$  I. Wts. and Acetic or Citric Acid mixed in solution set free Hydroferrocyanic Acid. In about a drachm of urine an acid pellet is first dissolved, next a ferrocyanide pellet is added; if albumin is present a precipitate is formed. Does not precipitate peptones. May also be applied as a ring test.

**Meta-Phosphoric Acid**,  $HPO_3 = 80.048$  I. Wts.—A fresh solution of a little of this acid is added to the clear filtered urine. A cloud or precipitation indicates presence of albumin.

**Millon's Reagent.—Nitroso-Nitrate of Mercury.** Mercury 10, Nitric Acid (Sp. Gr. 1.185) 25 by weight, Water 25. Dissolve in a flask at lukewarm heat, shaking often, and add to a solution formed by dissolving Mercury 10, in Nitric Acid (Sp. Gr. 1.25 to 1.3) 22 by weight without artificial heat. With albumin or urea this gives a yellow, then red colouration on heating.

### **Liquor Bellostii.—Syn. AQUA CAPUCINICA, MERCUROUS NITRATE SOLUTION.**

This consists of a 10% w/w Mercurous Nitrate Solution freshly prepared as follows:—Dissolve crystalline Mercurous Nitrate 1 Gm. in a mortar in a small quantity of Water with 2 drops of Nitric Acid. Make up with Water, added in portions, to 10 by weight.

Can be used to diagnose paralysis by boiling in a test tube a few Cc. of the urine in question, then without taking note of any precipitate that may have occurred one adds about 10 to 15 drops of the Reagent and boils again two or three times, taking care that the mixture does not 'bump.' Then allow to deposit. A white precipitate will be produced in all urines. In the case of paralytics, however, it will be gray to grayish-black and the supernatant liquid will be grayish-yellow.—Munch. Med. Woch. No. 1,1911. We have not experience of this test.

### **Nitric Acid Test.**

(See also Roberts' Test *infra* for modifications.)

Nitric Acid is placed in a test tube and the filtered urine, or diluted filtered urine, carefully 'layered' on to it. A white ring at the juncture of the liquids indicates presence of albumin; confirm by another reliable test. Not so delicate as the **heat and Acetic Acid**, but will show 1 in 12,000 at once. Bilious urines may produce play of colours characteristic of Gmelin's test. For *fallacies with the test*, vide below.

The test may also be applied by heat—i.e. add a little Nitric Acid mix and boil the upper portion.

**Glass Capsules of Nitric Acid** containing one minim are convenient.



Citric Acid 10 Gm. Water 7·5 Cc. may be used as confirmatory test. Apply by layering in similar manner—if mucus present the Citric Acid test will cause turbid ring.—M. 1906, 6.

In the Cold Nitric Acid Test *white rings more or less like albumin* rings are obtained by—

1. *Albumoses*.—These generally occur in association with albumin; should they occur alone, the ring with Nitric Acid will disappear with warming, to reappear on cooling, and there will be no cloud with the heat test.

2. *Bence-Jones's Albumose*.—This occurs with albumin, gives a ring with nitric acid that disappears on warming, to reappear on cooling; with the heat test a dense cloud appears at about 60° C. to disappear on further heating to boiling point. (*Vide* also p. 214.)

3. *Nucleo-albumin*.—The ring with this is not in contact with the nitric acid, but higher up and diffuse; it may be a real difficulty in diagnosis from albumin, for it is also precipitated by acetic acid, and may therefore give a cloudiness with the boiling test. The methods of avoiding this fallacy are mentioned under the Acetic Acid and boiling test.

4. *Urates*.—These may form a cloud near the Nitric Acid if the urine is very concentrated; the cloud will disappear on gentle warming, to reappear on cooling, so that it may also be mistaken for albumose; this fallacy may be avoided by diluting the urine with plain water before the nitric acid test is employed.

5. *Resins, etc.*, see next reference.—B.M.J.i./II, 417.

Copaiba Balsam, Sandal Oil and Turpentine—treated patients pass urine which cannot be tested for albumin with Nitric Acid as the whole precipitate—albumin and resin dissolve in the alcohol usually added to dissolve the resin. The addition of strong alcohol is however applicable if chromic acid be used as a test—also in case of patients treated with cubebs and coal tar. A false precipitation also occurs in case of patients treated with terpin hydrate.—L.ii./06 1459.

In lobar pneumonia, the urine gives a dense white or dirty white ring or only a haze *above* the junction of the urine and the acid by Heller's test. Sometimes it only appears after the urine has stood an hour or more, whilst in others it appears immediately. If the urine is turbid it must first be filtered. In cases where the reaction appears day after day the prognosis is favourable—if it disappears before the crisis or immediately after, unfavourable symptoms are experienced. The substance is apparently not of the known albumoses. The urine must be fresh.—R. C. Holt.—B.M.J. ii./10, 79.

### Picric Acid Solution.

Mann warns against the voluminous precipitate which one occasionally gets with Esbach's reagent giving a fictitious estimation. He says many albuminous urines give a pale blue with the **Biuret** reaction without any tendency to violet; others will give a reddish purple. Such urine indicates by the reddish color some hydrolytic change and will give the incorrect reading referred to.

Picric Acid 10 Gm., Citric Acid 20 Gm., dissolve in about 900 Cc. boiling water, cool and add water to 1,000 Cc. This reagent is used for the approximate determination of albumin by an Albuminometer which is about six inches long and 0·6 inch in diameter; the graduations on it are the results of experiment and indicate approximately 0·1 up to 0·7% albumin.

By comparison with a standard dried albumin solution, 1 in 1,000 and by heating to 180° F. and centrifugalising, the process can be terminated in a few minutes.

For exact determinations, albumin should be precipitated by some suitable reagent, itself nitrogen-free, *e.g.*, carbolic acid or tannin and the washed precipitate, dried and weighed, or better, the nitrogen contained in it should

be estimated by a Kjeldahl analysis, the amount of nitrogen found being multiplied by the factor 6.3 to obtain the amount of proteins.

N.B.—Methylene blue—in case of patients undergoing treatment with precipitates picric acid solution.—L. ii./o6,1459.

The administration of alkaloids may cause urine to give a precipitate with picric acid, but this is redissolved on heating to the boiling point.

**Roberts' Albumin Test.**—Nitric Acid 1 part, Solution of Magnesium Sulphate (10 in 13) 4 parts. Is found to be very satisfactory—advantage, high density. Slope the tube containing a little test solution and allow the urine to slowly run down into it with a dropper.

**A further modified Nitric Acid Test:—**

Ammonium Nitrate may be used instead of Magnesium Sulphate.

After obtaining ring shake slightly—the whole of the urine becomes turbid. This is not the case if ordinary Concentrated Nitric Acid is used, as turbidity dissolves at once.—J.C.S.A. ii./11,347.

**Salicyl-sulphonic Acid.**

$C_6H_3.SO_3H.OH.COOH = 218.118$  I. Wts.

In colourless crystals, prepared by action of sulphuric anhydride on salicylic acid. Soluble in water and alcohol. This test requires careful 'layering' of the urine upon a crystal, or a concentrated solution.

Is an extremely precise, reliable, and quick test, giving a dense white precipitate with all proteins except true Peptone. *Vide* below.

In confirmation note the following:—

Albumin, globulin, myosin, etc., coagulate on heating.

Albumoses dissolve on heating, and reappear on cooling.

Peptones are not precipitated, except in solutions saturated with ammonium sulphate.

Strongly recommended. Not affected by phosphates, bile, urates or alkaloids.—L. i./99,1085. Also by the late A. H. Allen.—P.J. ii./o4,9.

**NOTE.**—*Salicyl-sulphonic Acid does not precipitate pure Peptone but only the intermediate products between Albumin and Peptone.*

*Commercial Peptones, e.g., Witte's, contain considerable quantities of these and so give a positive reaction with Salicyl Sulphonic Acid. We had occasion to purify Witte's make by dissolving in Ammonium Sulphate to check accuracy of the test.*

**\*Endolytic Tubes (Albumin).**—Sealed Capillary tubes partially filled with a solution of this Reagent are portable for clinical use. The ends are snapped off and the urine (if necessary, filtered) is drawn into the tube by capillarity. From opalescence to thick precipitate occurs if positive. Distinguish albumose by pouring hot water over the tube—precipitate dissolves as above detailed. *Albumin and Glucose Endolytic Tubes* are also made. (pp. 204, 238.)

**Trichloroacetic Acid.** See Vol. I., p. 27. A saturated solution is used in the same manner as the last test, or a crystal may be used.

May precipitate uric acid and nucleo-proteids.

**Tannin-Hydrochloric Acid Test.**

Mix 5 Cc. of the specimen with 5 Cc. of 1.5% Alcoholic Tannin Solution warm, and add 5 Cc. of Dilute Hydrochloric Acid (1 in 3). Turbidity or yellowish precipitate. Interfering substances such as urates, phosphates and alkaloids are kept in solution by the acid and resins and alkaloids are redissolved by the alcohol and peptones by heating.



## Serum Globulin.

Globulin (held in solution by the salts) coagulates by heat and by Acids—readily soluble in an excess of Acetic Acid. The quantity of Globulin is usually extremely small, but in the advanced stage of many cases of Bright's disease, a marked and persistent increase in the proportion of it is a very unfavourable sign.

### Roberts' Test for Serum Globulin.

Add the serum drop by drop to a tall cylinder of water. Opalescence is produced, redissolving on addition of a little Acetic Acid or Liquor Potassæ.

### *To separate Serum Globulin from Serum Albumin—*

Faintly alkalise and then saturate with Magnesium Sulphate. Globulin is precipitated whilst the Albumin remains in solution. This may be made quantitative by operating on 100 Cc., collecting precipitate, washing with Magnesium Sulphate, dissolving in weak Saline, adding Acetic Acid (few drops) and boiling to coagulate, collecting, drying and weighing.—Mann.

**Globulins.** The protein of cerebro-spinal fluid is in the main globulin. In general paralysis the protein is increased, albumin is constantly present. The principal globulin in the fluid in general paralysis is EUGLOBULIN. It is the carrier of the interesting antibody operative in the Wassermann reaction (*q.v.*). Euglobulin differs from Serum Globulin in that it is precipitated in a 33% solution of Ammonium Sulphate, whilst 50% is necessary to precipitate Serum globulin.—L. ii./09,210.

When small quantities only are available, as often in lumbar puncture, add a few drops of cerebro-spinal fluid to the following solution freshly made:—(Spiegler's) Mercuric Chloride 4, Tartaric Acid 2, Glycerin 10, Distilled Water 100. This gives a cloudy precipitate with only traces of Protein; specially sensitive to Serum Globulin.

## Albumoses.

**To detect Albumoses.**—Acidulate the specimen with Acetic Acid, add 10% Potassium Ferrocyanide Solution. This precipitates primary Albumoses. This ferrocyanide precipitation distinguishes albumose from *Compound protein*. On warming the precipitate dissolves, to reappear on cooling. This distinguishes from that due to Serum Albumin.

Albumoses dissolve on heating (after precipitation by a reagent, *e.g.*, salicyl-sulphonic acid) and reappear on cooling. What was formerly called '**peptone**' should really apply to albumose. True peptones (true albuminous substances not precipitated by salting with Ammonium Sulphate) do not occur in the urine.

May safely regard all proteins in urine as albumoses, which dissolve, and reappear on cooling, as above mentioned.—L. i./09,682.

**Biuret Reaction.**—After testing for albumin in the usual way, with the Nitric Acid ring method, this is removed if present by 10% Trichloroacetic Acid Solution, and the filtrate then tested with the Biuret Test. The author employed this as follows:—

In a test tube place 1 drop of Copper Sulphate Solution (2%), add 5 Cc. urine, then 5 Cc. of Sodium Hydroxide Solution (10%). A rose pink indicates the presence of albumose.—L. i./09,682.

**Albumose** (Bence Jones's) occurs in myelopathic albumosuria, a disease associated with morbid conditions of the bones, *vide* B.M.J. ii./o6, 1442. This albumose is detected by (1) coagulating at 58° C. *i.e.*, lower than serum albumin, which coagulates at 75° C., (2) precipitates with *hydrochloric acid*, (3) nitric acid in the cold—on raising to the boiling point, however the coagulum dissolves more or less completely and reappears on cooling, (4) with potassium ferrocyanide and citric acid (often takes time to develop, differing in this respect from albumin). The hydrochloric acid test is exceedingly sensitive and does not depend on excess of salts. The result is obtainable after very free dilution of the specimen.

**Bence-Jones' Proteinuria.**—Note on a case of (chronic nephritis). The urine gave abundant precipitate on applying the ordinary heat test for albumin and rather curdy precipitate at once at well below the boiling point with partial solution on boiling,—completely soluble on addition of a drop of 10% Acetic Acid. On contact with Nitric Acid in the cold a copious white precipitate formed which disappeared on warming and reappeared on cooling. Ordinary albuminous urine coagulates about 70° C. with no tendency for the coagulum to disappear on raising to the boiling point. In this case, however, coagulation began at 52·5° C. and was complete at 58° C. Ordinary Protein tests were +, *i.e.*, Biuret (marked) 'Millon' and tryptophane reactions.—L. i./13,522.

### Amino-Acids.

**Estimation of Amino-Acids in the Urine.** P. J. Cambridge estimates the Ammonia present by Folin's method and the Ammonia *plus* Amino Acids present as indicated by Malfatti's process and deducts the first from the second result to give the amount of Amino-Acids present.

**Folin's Method** consists in aspirating the ammonia formed from 25 Cc. of the urine with about 1 Gm. of Sodium Carbonate through 25 Cc. N/10 Sulphuric Acid containing a few drops of Alizarin Red as indicator, for two hours. The non-neutralised acid is then titrated with N/10 Sodium Hydrate. The difference gives the amount of acid neutralised by the Ammonia in 25 Cc. of the urine—this multiplied by 0·0014 Gm. gives Ammonia Nitrogen.

The **Malfatti process** depends on the fact that Ammonia Salts react with Formaldehyde in neutral solution to form Hexamine, setting free the Acids with which the Ammonia was combined. These can be titrated with alkali.

10 Cc. of urine are diluted with about 50 Cc. of Ammonia-free Water and 3 or 4 drops of Phenolphthalein Solution added. Neutralise with N/10 Sodium Hydrate and note quantity required. 3 Cc. of Neutral Formaldehyde solution are added (pink colour disappears). N/10 Sodium Hydrate is again added to neutralise and the quantity noted. The difference between the first and second readings multiplied by 0·0014 Gm. and the result by 10 gives the percentage of 'Ammonia' Nitrogen. From this the content of 24 hours urine is calculated. Amino-acids react like Ammonia to Formaldehyde so that the result by the Malfatti process is the sum of Ammonia plus Amino-Acids present as already stated.

The amount of Amino-Acid Nitrogen in simple cases of glycosuria may be nil by the method described, except where there is evidence of a gouty condition or serious hepatic derangement, then there may be 0·5 Gm. in 24 hours. When secondary disturbances of metabolism occur the Amino-Acid Nitrogen is small at first, 0·05 Gm.



or less. It generally increases rapidly, often more so than Acetone, until 2 Gm. or more is being eliminated. Finally it may be present in such amount that Tyrosine crystallises out.

The appearance of Amino Acids in the urine in diabetics is usually a sign that more Carbohydrate is being consumed than the patient can deal with efficiently. Careful dieting to reduce it will effect prolongation of life.—P. J. Cammidge, L. ii./13,1319.

### Abderhalden's Serum Reaction.

Abderhalden demonstrated the capacity of the Blood Serum during pregnancy to break down placental albumins and peptones.

It has been shown that similar reactions are obtained with blood serum from females suffering from genital growths, also that albumins from placenta, uterus, ovaries, genital neoplasms and to a less degree muscles are similarly broken down—the reaction being general rather than specific.—B.M.J. ii./13,183.

**Ninhydrin.**—Triketohydrindene Hydrate for Abderhalden Serum Reaction.

When heated to boiling in aqueous solution (1%) in presence of Protein bodies or certain Amino-Acids this body gives a bluish violet colour. Hence used as a test for Albumin, Peptone, Polypeptides and Amino-Acids. Especially to demonstrate in Blood Serum presence of specific proteolytic ferments, in particular in diagnosis of normal pregnancy. In cases of carcinoma and fever the reaction may be doubtful.—Jl. A.M.A., 1912,1377; B.M.J. ii./13,1004.

Technique of the Reaction.—W. E. Bullock, L. ii./14,225.

Negative results with the reaction as a test for Amino-Acids in serum of nephritics and others. A few tests were made with ascitic fluid with negative results.—R. M. Pearce, J.A.M.A., 1913,1456.

Abderhalden's method in diagnosis of carcinoma. A paper demonstrating the possibility of the existence of a specific ferment against carcinomatous tissue in diagnosis of carcinoma. The blood of persons suffering from carcinoma contains a substance absent in the blood of all others having a proteolytic action on carcinoma tissue only. Several factors point to it being of ferment nature.—L. ii./13,1385. See also L. i./14,1411.

**Placentin** as cuti-reaction in pregnancy.—B.M.J. i./14,833. *c.f.* Animal Organotherapy, p. 136.

Albuminuria in pregnancy, significance of. A marked increase in cases of post-partum hæmorrhage found, not necessarily in eclampsia, but in cases of albuminuria.—B.M.J. ii./12,1009; see also L. i./13,1366.

### Bile.

(With some notes on further abnormal constituents.)

**Nitric Acid** (Sp. Gr. 1.420 is best, W.H.M.) *i.e.*, **Gmelin's Test** produces a bluish-green ring and play of colours.

A moderately icteric urine diluted even 1 in 50 will give this usually.—W.H.M. on application of.—C.D. i./03,171.

**Peptone Test.**—Peptone, in powder 30, Salicylic Acid 4, Acetic Acid 30, Distilled Water 3,500.

Dissolve and filter. Add 1 of urine containing bile salts to 2 of this solution opalescence (or p.p.) appears; it dissolves completely on adding acetic or citric acid, and diminishes, but does not disappear on boiling.—*Oliver*.

**Sulphanilic Acid.** (*Vide* also Vol. I., p. 273).

1% Solution with Sodium Nitrite 1% and Hydrochloric Acid as a test for bile pigments.—L. i./06,923.

For further details of the test, *c.f.* M.L. 1906, p. 17.

**Tincture of Iodine.**—A few drops “layered” on to the specimen and the tube shaken gently, produce a green colour if bile pigment be present.

**Pettenköfer's Test for Bile Salts.** Add a few drops of Syrup, shake, and then Sulphuric Acid.—Reddish-violet colour, *c.f.* **Acid Cholalic and Sodii Taurocholas in Organic Analysis Chart.**

**Chromic Acid.** 5% solution added gradually produces a green colour.

**Sodium Nitrite** with Sulphuric Acid (Vitali's Reaction) gives green colour.

The spectroscope is employed for detecting **Urochrome, Urobilin, Hæmatoporphyrin, Uroerythrin.**

Urine of patients taking Trional, Tetronal and Sulphonal should be watched for possible hæmatoporphyrinuria.

An account of a case exhibiting.—*L. ii./12,960.*

Hæmatoporphyrinuria does not alone account for the altered color of the urine.—*L. i./09,1106.*

### **Urobilin.**

Simple test for (Schlesinger). To the unfiltered urine add alcoholic solution of Zinc Acetate 1 in 10. Shake and add a few drops Lugol's Solution. Fluorescence in varying intensity indicates presence.—*B.M.J. ii./08,1357.* Has been used as a test for Malaria, *q.v.*

**Urobilinogen.** This body is stated to be the parent of Urobilin (*v. above*). Urobilin is formed from it on standing exposed to the atmosphere.

**UROBILINOGEN TEST (P.G.V.):**—Dimethylparaminobenzaldehyde  $C_6H_4N(CH_3)_2.CO.H$  (1:4) M. Pt.  $73^{\circ} C.$  2, dissolved in 98 of a mixture of Hydrochloric Acid 4 and Water 1. (*c.f.*, Ehrlich's Indican Test, p. 243). It will be seen that the parent substances of Indican *viz.* Indol  $C_8H_7N$  and Indoxyl  $C_8H_5(NH)OH$  bear relation chemically with the bodies contained in Urobilinogen *viz.*, Bilirubin  $C_{32}H_{36}N_4O_6$ , Hydrobilirubin  $C_{32}H_{40}N_4O_7$ , etc.

Diagnosis of commoner cases of chronic jaundice. Examination of the urine should be as complete as possible, *e.g.*, test for bile (Gmelin's test is best), for Urobilin (by Alcoholic Zinc Acetate Test), Indican, Sugar (“the presence of this in a case of chronic jaundice is almost pathognomonic of serious disease of the pancreas which may be malignant or inflammatory.”) Glycosuria was met with by the author of this paper in 7.5% cases under his care,—(it occurs with almost the same frequency in cancer of the pancreas and in jaundice due to gall-stones,—8% and 9% respectively). Conduct the “pancreatic reaction” (positive reaction obtained in 64% of cases of chronic jaundice), examine for fats, intestinal putrefaction, color, etc.—*P. J. Cammidge, B.M.J. i./11,486.*

**Cholesterin (q.v.)** is rarely found. It is usually derived from a collection of pus that has been retained in a cavity for some time, ultimately discharging into the urine. A few recorded cases are detailed.

To separate cholesterin extract the specimen with alcohol-free Ether. Purify the residue on evaporation by dissolving in strong alcoholic potash, evaporating, extracting again with Ether, and this again with boiling alcohol—rhombic plates.—*Manu.*

Chloroformic solution of Cholesterin with Sulphuric Acid gives a red to purple colour. An Alcoholic solution so treated gives red to blue.

Cholesterin crystals in urine, in diabetes with neuritis, in cystitis, in Bright's disease, in pyonephrosis, in epilepsy in a case of hæmaturia with fibrous casts, in tabes and lipuria, in fatty degeneration of the kidneys.—*B.M.J. i./03,1008.*

### **Tyrosin, $\beta$ -Oxyphenylalanin- $\alpha$ .**

$C_6H_4.OH.C_2H_3(NH_2).COOH = 181.098$  I.Wts.

Is recognised by its characteristic crystalline appearance being in shining needles, either in bundles or star form.

Synthesis of, from Potassium Cyanide.—*L. ii./06,1583.*

**Russula delica.**—The juice of this fungus is a test for Tyrosin; changes it from red to black.

The fungus has stem short 1 to 2 ins. high,  $\frac{1}{2}$  in. or more thick, even, smooth, white cap, fleshy, 3 to 5 ins. broad, funnel-shaped when full grown, regular, even, smooth, margin involute, without striæ, flesh firm, dry, white.

Enzymes as Reagents.—*Y.B.P. 1907, 55.*

### **Further Tests for Tyrosin.**

Two Cc. of Sulphuric Acid mixed with 3 to 5 drops of a Solution of Aldehyde in twice its volume of Alcohol 90%, care being taken that the liquid

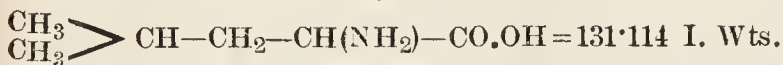


remains colourless—a few drops added to the suspected liquid produces a gooseberry red colour. This test is supposed to detect Tyrosin up to 1 in 10,000.

Piria states on adding a few drops of strong Sulphuric Acid to a little Tyrosin in a dish it dissolves with slight reddening, on saturating with Barium Carbonate (after diluting) and adding to the filtrate neutral Ferric Chloride Solution a violet colour is formed.—Schmidt.

**Ammonium-Sulpho-Molybdate**, *q.v.*, gives blue to violet colour.

**Leucin**  $\alpha$ -Amido iso-caproic Acid.



**Leucin** occurs as an early result of protein cleavage. There are two isomeric forms of it—respectively *laevo*- and *dextro*-.

Is in crystalline spheroidal clumps. An arterial depressor. Is given in arteriosclerosis.—B.M.J. i./o6,126.

### Blood Corpuscles

may be recognised microscopically. The red blood corpuscle has an average diameter  $7.5 \mu = \frac{1}{3388}$  inch. It is discoid in shape with indentations in the two sides. Occasionally it is smaller, *e.g.*,  $6 \mu (= \frac{1}{4200})$  inch. Price-Jones determined in normal human blood diameter to be  $6 \mu$  to  $8.75 \mu$ —with an average of  $7.4 \mu$ , whilst in pernicious anæmia the diameter varied from  $4 \mu$  to  $11.75 \mu$ , and the average diameter of five successive 100 cells was  $8.0 \mu$ .—B.M.J. ii./10,1418.

In disease it may reach 8 to  $10 \mu = \frac{1}{2575}$  to  $\frac{1}{2540}$  inch, *i.e.*, ANISOCYTOSIS, or irregularity in size; further in disease the corpuscles may exhibit POIKILOCYTOSIS, *i.e.*, irregularity in shape. In examination of films VACUOLATION should be noticed, as also irregularity in staining (POLYCHROMATOPHILIA). With regard to abnormal red cells—these are mainly of two kinds, (1) those like normal cells without nuclei, (2) nucleated. The group (1) where they have special designations have names ending in *cyte* (*microcyte*, *megalocyte*, etc., based on the type of the normal corpuscle which is called *erythrocyte*), whilst the nucleated forms have names ending in *blast*. In this group are *normoblasts*, *megaloblasts*. For morphological details and significance we may refer to Emery or other text book.

#### The Structure of the Red Blood Corpuscle.

“It would seem that there is some outer structureless material on a red corpuscle that is removed by strongly acid pepsin solutions. Inside this lies the true envelope of the red cell, devoid of histological structure, capable of coalescing with similar material in other red cells to form a bigger mass, and capable of fractionation into smaller masses. Within this again is the hæmoglobin, not in watery solution, perhaps linked to the envelope by lecithin. And within the capsule of envelope and hæmoglobin lies the material that is extruded to form the blood platelets, perhaps also the bodies which exhibit Brownian movements in fresh preparations of living blood and the so-called ‘spirochaetes’ of normal blood.”—E. M. Brockbank.—B.M.J. ii./13,1104.

For details of **white corpuscles** *v. p.* 222.

**Precipitin Test for Blood.**—Precipitins are formed when the serum of one kind of animal is introduced into the body of another species, *e.g.*, the serum of a horse injected into a goat causes the serum of the goat to be capable of forming a precipitate with normal horse serum.

In using the test for forensic purposes a rabbit is injected with defibrinated human blood. The serum of the rabbit ‘**anti-human serum**’ when dropped into a clear solution of human blood causes a precipitate,—not in solution of blood from another animal. The principal difficulty in the test

is to obtain from the rabbit an antihuman precipitating serum of the proper strength. To be thoroughly reliable and specific *the formation of the precipitate must begin in five minutes and be complete in thirty minutes.* Old blood stains respond as well as recent. It has been stated that the blood of mummies, 3,000-5,000 years old could be identified as human by the method.—*L. i./ii,319.*

Examining mosquitos which had been in contact with certain animals it was possible to determine with accuracy the species of the animal each mosquito had bitten and to prove absence of human blood.—*B.M.J. i./io,85.*

The test was employed in the Clapham murder case. A human blood stain taken up with normal Saline and some anti-human Serum added causes a white cloudy ring.—not so the stains from animal blood. Specific sera injected into a rabbit form an equally specific anti-serum—in other words, human anti-serum, will infallibly detect human blood,—a horse anti-serum will detect horse's blood and so on.—*P.J. i./ii,202.*

**INTERPRETATION OF THE REACTION.**—An investigation dealing with the weights of the precipitates,—the main mass of the precipitate appears to be composed of anti-substance (Precipitin).—*B.M.J. ii./io,1511.*

Indian experience with the test was that it is absolutely trustworthy,—the reaction is not effected by the decomposition of the blood, by heat, etc. Fowl's blood used instead of rabbit's. Failures with goat's and monkey's blood.—*B.M.J. i./ii,1481.*

**Hydatid Fluid** may be used to give precipitin test as aid in diagnosis. Interaction between hydatid fluid and serum from hydatid patients has been obtained.

In the rarer cases where the echinococcus has invaded bone structures diagnosis is difficult. The hydatid fluid must be fresh for the test. The presence of eosinophilia is a useful help to diagnosis.—*B.M.J. ii./09,957.*

**Hydatid disease.** Complement—fixation as mode of diagnosis. Found to be of considerable value in the few cases available,—positive results are conclusive, negative difficult to interpret. Modified Hecht method used. The alcoholic heart muscle being replaced by Hydatid Fluid of the sheep as antigen. Hitherto the method of diagnosis has been the verification of eosinophilia,—this is, however, characteristic of almost every form of vermiform parasite.—*L. ii./io,377.*

**Blood in Urine.**—To test for, heat the specimen with strong potash or soda. If present a colour described as bottle-green is produced, and earthy phosphates coloured brownish-red by blood are precipitated.

**Ozonic Ether and Guaiacum Test** for,—add a drop or two of *fresh Tincture of Guaiacum*—Guaiacum Resin 1, in Alcohol (90%) *q.s.* to 10—to a small quantity of the urine and shake, 'layer' Ozonic Ether on to the mixture. A blue colour at once, or on standing, indicates presence of blood—Iodine in the urine also gives this colour (*e.g.* if patient has been treated with iodides). Further, pus gives it with Guaiacum Tincture alone, the colour disappearing on heating.

Reactions of Hæmoglobin to the Guaiacum test discussed.—*B.M.J. i./06,75.*

#### **Modified Guaiacum Test using Sodium Perborate.**

To about 5 Cc. of the liquid add 1 to 5 drops of Alcoholic Solution of Guaiacum Resin (saturated in the cold, and not more than 12 hours old), then about 1 Gm. Sodium Perborate and about 10 Cc. of 30% Acetic Acid, shake the mixture once and pour Alcohol carefully into the tube to form a separate layer,—a blue or blue-green color at the junction in five minutes will be formed, or green if only a trace. The test is said to show 0.035 Gm. of blood in a litre of water. The Guaiacum resin used must show a brown, not a greenish fractured surface.—*P.J. ii./io,365.*

*In our laboratory we found this to indicate 0.02 Gm. of blood per litre, i.e., 1 in 50,000. It is about five times as delicate as the Ozonic Ether Test. A green colour should be disregarded as we found a blank test gives a green. Fresh Solution of Guaiacum had no advantage over seven months old Simple Tincture of Guaiacum.*

**Benzidine**—Saturated Alcoholic Solution—a few drops added—shaken and 'layered' with Ozonic Ether forms blue ring at once. *Vide* also below.

**Blood, Recognition of, in Stains.**—Plunge the cloth into boiling water for a few minutes, place on slide and add few drops of Ammonium Sulphide. Examine microspectroscopically for absorption bands of



**hæmochromogen.** May be increased by 10% Potassium Cyanide Solution. If on a weapon or piece of jewellery, moisten with Ammonium Sulphide and scrape off sufficient and examine as before.—B.M.J. ii./06,1261.

**Oxyhæmoglobin** in solution with a little Sodium Chloride evaporated over Sulphuric Acid to syrup consistence. Mixed with fifteen times volume of Glacial Acetic Acid and heated on a water bath several hours yields, on cooling, flat rhombic crystals of Hæmatin Hydrochloride with dark violet colour and lustre—this is one of the recognised tests for blood stains.—B.P.C.

Cases of intracorpuseular sulph-hæmoglobanæmia (*enterogenous cyanosis*) probably due to increased formation of sulphuretted hydrogen in the intestine.—L. i./07,275.

**Blood Stains on Clothing, etc.**—The Guaiacum Test is highly spoken of. The stain must give a red aqueous extract yielding no colouration to a straw-coloured solution of Guaiacum in alcohol 90% when applied by itself but a blue colouration within one second on further addition of Hydrogen Peroxide. Oxidisers and enzymes give a reaction with Guaiacum Solution alone. Blood does not.—Analyst, 1912; Y.B.P. 1913,40.

**Recognition of Blood Stains.**—Chloral Solution to extract blood stains. The stain is moistened with Acetic Acid and then soaked in a 70 to 80 per cent. solution of Chloral Hydrate for one or several hours if necessary. To the solution add a few drops of the Reagent (Guaiacum, Barbaloin, or Benzidine), then add Hydrogen Peroxide 10 volume strength diluted with double volume of Alcohol and slightly acidified with Acetic Acid (carefully superposed). The presence of Pyridine greatly accelerates and intensifies the reactions.—P. J. ii./12,158.

**Benzidine.** *Syn. p-Diamidodiphenyl.*— $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{C}_6\text{H}_4 \cdot \text{NH}_2 = 184 \cdot 116$  I. Wts. Grey crystalline powder soluble in alcohol, is used as blood test. Mix the specimen with a little hydrogen peroxide, add a few drops of Acetic Acid and then a little Benzidine Solution—if present blue to green colour.—M./06,55.

We found that a dilution of blood 1 in 200,000 gave a distinct bluish-green color on adding  $\frac{1}{2}$  Cc. of 1% Solution of Benzidine in 50% Acetic Acid to 1 Cc. of the dilution.

Commercial Benzidine should be tested before use for the blood reaction. A saturated solution of Benzidine in Alcohol is rendered acid with Acetic Acid, or a saturated solution of Benzidine in Glacial Acetic Acid is mixed with an equal quantity of Hydrogen Peroxide, and a few Cc. of Water added. No coloration or only a slight one should occur in a few minutes.—M. 1910, 141, per P. J. ii./10,492.

Diastases, Zymases, Fruit Juices give similar reaction. A positive reaction does not prove blood, but the negative proves its absence.—P. J. ii./10,298.

Tablets may be made of Benzidine 0.1 Gm. and Sodium Perborate 0.1 Gm. (better than  $\text{H}_2\text{O}_2$ ). Just before use dissolve a Tablet in 10 Cc. Glacial Acetic Acid. If a suspected spot on an article of clothing, etc., is to be examined, it is moistened with a drop of Normal Saline and well rubbed with a glass rod. The drop is then absorbed in a small piece of absorbent cotton wool and the spot at once treated with a few drops of the Reagent. In presence of blood a blue color is seen.—J.C.S.A. ii./10,665.

**FÆCES, TESTS FOR OCCULT BLOOD IN,**—(1). Modified Benzidine, (2). Aloin Test, (3). Guaiacum Test,—P. J. Cammidge.—B.M.J. ii./10,409. See also Fæces.—p. 235.

**Choline.**—Halliburton and Rosenheim's Test for in the Blood and Cerebro-spinal Fluid.—Dark brown crystals (Choline Periodide) resembling hæmin appear on adding a strong solution of Iodine in Potassium Iodide to Choline-platino-chloride crystals. To prepare the Platino Chloride of Choline is, however, not essential, as the test can be applied direct to the Alcoholic Extract of the fluid.

Acetyl-Choline (artificial) has a powerful depressing action on blood pressure, being capable of overcoming the effects of Adrenalin.

Chemistry of the blood,—some notes on—Na. Aug. 1911, p. 204.

The **Marchi Reaction** is now generally in use for showing nerve degeneration. The reaction consists in the fact that the fatty acid (decomposition product of Lecithin) stains black with Osmic Acid even in the presence of Chromic Salts which Lecithin does not.

In degenerative nerve disease,—the products, notably Choline, can be detected in the blood and cerebro-spinal fluid. This fact might be used for diagnosing between functional and organic disease.—L. i./07,1303.

**Blood, Estimation of Hæmoglobin.**—Sir Wm. R. Gowers' apparatus consists of two tubes, flattened or round, one closed, containing glycerin jelly coloured with picro-carmin—the standard equal to the colour of a dilution of average normal blood one hundred times (20 cmm. in 2 Cc.) and the other, graduated in 100 degrees = 2 Cc., for the dilution of the sample of blood with distilled water. The outfit further includes a pipette, pricker, india-rubber stand, &c.

The lobe of the ear or the finger is pricked and 20 cmm. of blood are drawn up into the pipette, injected into the graduated tube, which should at the time contain a few drops of water to prevent possible coagulation and facilitate mixture. Water is then added sufficient to produce a tint the same as the standard, the two being frequently compared during the process. The degrees of dilution needed indicate the percentage amount of hæmoglobin. For example, 20 cmm. of blood from an anæmic patient giving the standard tint at 30 degrees of dilution would contain only 30% of the normal quantity of hæmoglobin.

**Haldane's Modification** of Sir W. Gowers' Hæmoglobinometer is now extensively used where coal gas is available. The standard tint tube is a 10% solution of blood containing the average percentage of hæmoglobin found in the blood of healthy adult men, and having an oxygen capacity of 18.5% as determined by the ferricyanide method. *The solution is saturated with carbon monoxide*, and hermetically sealed. It is both definite and permanent. The graduated tube holds 2 Cc. when filled so that the inside is completely wetted and the liquid stands at the mark 100 after half a minute has been allowed for the upper part to drain. The tube is graduated in percentages of 2 Cc.

A cap for attachment to a gas-burner serves to deliver gas for saturating the diluted blood with CO.

The advantages of the modifications are: (1) that the standard solution is a definite one, so that an instrument can be verified at any time by making a determination with ox-blood of which the oxygen capacity has been determined by the ferricyanide method: (2) that the standard solution is permanent; (3) that the apparatus can be used with equal correctness by daylight and artificial light.

As coal-gas is not always available in examining the blood of patients the instrument can always be supplied with an additional standard tube containing picro-carmin jelly, as in the original Gowers' Hæmoglobinometer. The picro-carmin jelly is standardised to correspond with blood of 18.5% oxygen capacity, but is liable to slow alteration on keeping. Its value in terms of the sealed tube of blood-solution should therefore be occasionally ascertained by determining the hæmoglobin in blood from the same person, first by the picro-carmin standard and afterwards by the sealed blood standard. The difference gives the percentage correction needed for the picro-carmin standard. The picro-carmin standard tube should be kept in the box, and not exposed unnecessarily to light.

Other Hæmoglobinometers are Oliver's, Fleischl's and Sahli's Hæmometer.

Sahli's is unreliable owing to acid hæmatin, the standard employed, not being stable, the substance deposits in time. The Gowers-Haldane Instrument *vide* above, is the best.—B.M.J. i/11, 1474.

**Hæmoglobin Scale** according to Tallquist consists of a scale with strip of blotting paper to suck up the blood for examination. The tint thus produced is compared by direct light with the scale. The scale indicates 10, 20, 30, &c., up to 100. This refers to amount of hæmoglobin—100 being taken as normal.

**Rotary Hæmoglobinometer.** A. J. Hall devised an instrument on similar lines. For directions for use, *vide* L. i./09, 696.

**Blood, Number of Corpuscles.**—One cubic millimeter contains normally about 5,000,000 to 6,000,000 red corpuscles in man, and about 4,500,000 in woman. The average number of white corpuscles per cubic millimeter is about 7,000 to 8,000 in adults, and 10,000 in children.

The hæmacytometers chiefly employed are Gowers' modification of Hayem's, and that of Thoma-Zeiss.

In the **Gowers Instrument** the cell is  $\frac{1}{2}$  mm deep, and each side of a square is  $\frac{1}{10}$  mm., hence the volume of the small square is  $\frac{1}{500}$  cmm. This instrument contains, in addition to the cell, a small pipette which, when filled to the mark on its stem, holds exactly 1.995 cmm., a capillary tube marked to



contain exactly 5 cmm., a glass stirrer, a lancet, needle, &c. The dilution employed is 1 to 200. The number of corpuscles in 10 squares is counted, and this multiplied by 10,000 gives the number in a cubic millimeter. The above dilution and squares are so arranged that normal blood presents 50 corpuscles per square, or 100 in 2 squares; and by counting 10 squares so as to get the average for two, the *percentage* of corpuscles to that of health is evident, and may be compared with the percentage of hæmoglobin as ascertained by Sir Wm. R. Gowers' hæmoglobinometer, *v. p.* 220.

If, for instance, the blood contain 80% of corpuscles and only 40% hæmoglobin, the value of each corpuscle is represented by the fraction  $\frac{1}{2}$ . Sometimes in pernicious anæmia the corpuscles sink below the amount of hæmoglobin, and there may be 30% of corpuscles and 40% of hæmoglobin, in which case the value of the corpuscle is  $\frac{2}{3}$ . The corpuscles having settled, and the percentage ascertained, the objective may be raised so that the corpuscles are somewhat out of focus, the *leucocytes* then appear as bright points, in consequence of their greater refraction, and their number may be counted. Sir Wm. R. Gowers prefers this method to that of staining.

The **Thoma-Zeiss** instrument consists of micrometer slide divided into 16 squares, each square again divided into 16 smaller squares. It has two pipettes, one for diluting the blood 1 to 100 and 1 to 200 for counting the red corpuscles, the other is intended for estimation of the leucocytes, and dilutes the blood 10 or 20 times. The number of red corpuscles seen in 4, 6, or if greater accuracy is required, 16 (larger) squares, *i.e.*, in 64, 96 or 256 smaller squares, is counted. To ascertain the **number of Red Corpuscles** in 1 cmm. of blood, knowing the volume of the cube standing on each small square to be  $\frac{1}{4000}$  cmm., *multiply the total number of red corpuseles counted by 4,000 times the number of times of dilution of the blood and divide the result by the number of small squares in which red corpuscles have been counted.* It is always desirable to have an assistant to note the numbers observed, and to count the corpuscles touching and overlapping the two adjacent boundary lines on the left upper corners of the squares, but those on or overlapping the other two sides are excluded to compensate.

The normal dilution is 1 to 200; in polyemia 1 to 400; and in excessive anæmia 1 to 100 may be used. 5 or 6 corpuscles per square are a convenient number for counting.

The Thoma-Zeiss cell is  $\frac{1}{10}$  mm. deep and each side of a small square is  $\frac{1}{20}$  mm., hence the above figure  $\frac{1}{4000}$  cmm. as the volume of a small square.

The fluid used for diluting in both the above instruments is **Sir Wm. R. Gowers' Hæmacytometer Solution**:—Sodium Sulphate 104 grains, Acetic Acid 1 drachm, Distilled Water 4 ounces. Filter.

**Hayem's Solution** is also employed. Sodium Chloride 2, Sodium Sulphate 5, Mercuric Perchloride 0.5, Water 200.

*Correction of Error with formulæ.*—B.M.J.E. i./o8,12.

**Edington's Hæmacytometer Solution**.—Sodium Citrate (neutral) 7.5 Gm. Formalin (40% Commercial), 2.0 Cc. Dahlia (Methyl Violet), 0.03 Gm. Chloroform 5 drops, Distilled Water 250 Cc. Mix the stain with the water, then add the Sodium Citrate and the Formalin. Has the advantage that in less than 1 minute, all the corpuseles are deposited on the slide and in focus. The refractive index of the corpuscles is well maintained.—L. ii./o7,86.

The **Ehrlich Blenden Eyepiece** is stated to simplify counting either red or white corpuscles. It consists of an ordinary No. 2 eyepiece with a screen which cuts out a square from the field of vision. The number of corpuscles seen per square (average of several counts)  $\times 4000 \times$  the dilution (1 in 100 or 1 in 200) gives the number per cubic mm.—L. ii./o9,1424.

**Estimation of Red Corpuscles** by means of the **Hæmatocrite** (not satisfactory for the white). This instrument consists of two graduated capillary tubes in a metal frame for inserting in a centrifuge to be revolved at high speed. The finger is pricked after cleansing with carbolic solution; the first drop of blood is rejected—this is important—and the next exuding is taken up into both tubes by capillarity; it is then centrifugalised for one minute with 10,000 revolutions. The red corpuscles having the higher sp. gr. are separated at the distal extremity of the tube. Normal blood should reach the mark 45 to 50, indicating 4,500,000 to 5,000,000 corpuscles per cubic m.m. Taking the 5,000,000 as a standard, if the corpuscles reach the mark 25 this indicates a percentage by volume 50 or 2,500,000 red corpuscles per cubic mm.

The '**Color Index**' is the index of corpuscular richness. It is obtained by dividing the percentage of Hæmoglobin by the percentage of Red Corpuscles.

With the normal of Red Corpuscles as 5,000,000 and the Hæmoglobin at 100 the index is  $\frac{100}{5000} = 1$ . In a case of Red Corpuscles 4,000,000 (=80% of normal) and Hæmoglobin 40%, the index would be  $\frac{40}{4000} = 0.5$ . Consult Emery, p. 192 for importance of this index in differentiating chlorosis, pernicious anæmia and in other types of anæmia.

**The Number of Leucocytes** may be estimated in a similar manner, by the Thoma-Zeiss instrument, but in this case it is desirable to stain them before counting by using Gowers' diluting fluid, with an appreciable addition of Löffler's Methylene Blue, or by Toison's Solution (Dissolve Methyl Violet 5 B. 0.025 Gm. in a mixture of Glycerin 30 Cc. and Water 80 Cc. Dissolve separately Sodium Sulphate 8 Gm. with Sodium Chloride 1 Gm. in Water 80 Cc. Mix and filter). Leucocytes stained violet, red corpuscles greenish. For accuracy count as many squares as possible.

A further formula for the staining fluid is Formalin 1.5, Sodium Chloride 0.5, Sodium Sulphate 2.5 Methyl Violet 0.01, Water 100.

Another method is to use an aqueous  $\frac{1}{4}\%$  acetic acid solution as diluent, in this the red corpuscles become invisible while the leucocytes remain visible (Thoma-Zeiss).

In **Leucocytosis** the number of white corpuscles may be increased from the normal 7,000 or 8,000 up to 12,000, or even to as many as 1,000,000 per cubic mm.—L. i./03,361.

### Leucocytes in Normal Blood.

- (Regular Nuclei.) (1). Lymphocytes, small, } 25% (L.).  
large }  
(In childhood more numerous,—up to 60%.)  
(2). Hyaline (large Mononuclear Cells) 1 to 2% (H.).  
(3). Transitional Cells 1 to 2% (T.).  
(Irregular Nuclei.) (4). Polymorphonuclear neutrophils 70 to 80% (P.).  
(In childhood only 30 to 40%).  
(5). Oxyphile cells (Eosinophile Leucocytes) 3 to 5% (E)  
(6). Basophile Cells (Mast Cells) 0.5% (B.).  
(Often not found in persons in robust health.)

The cells comprised in Nos. 1 to 3 are sometimes called the non-granular whilst those in 4 to 6 are called the granular leucocytes, *i.e.* they contain granules in their protoplasm. The initial letters are commonly used for counting purposes. For an account of Recent Advances in Hæmatology see W. K. Hunter (The Dr. James Watson Lectures) Glasg. Med. Jl. vol. LXXIV. *et seq.*

Consult also Green's Encyclopedia, Emery, etc. For the method of differential counting of the Leucocytes and signification of data in disease, Emery's work may well be used.

**Strong's Method.** The stain is composed of Methyl Violet 0.012 Gm., Sodium Chloride 0.75 Gm., Formalin Solution 1.5 Cc. Distilled Water 100.0 Cc.

A new method of blood-counting producing permanent preparations which may be used subsequently. Eliminates ruled counting chamber and error due to variations in the depths of the cells.—B.M.J. ii./03,74.

Enumeration of leucocytes after staining by Leishman's stain (*v. infra*).—Leishman. B.M.J. i./06,680.

**Leucocytes, Improved Method of Counting.** To stain a 3% sodium chloride solution deeply coloured with Gentian Violet is sufficient. It is simpler to count whole microscopic fields of known area rather than squares. Employing the 1 in 20 pipette, count whole microscopic field, not the squares, move the draw-tube of microscope into such position that  $7\frac{1}{8}$  squares in diameter (Thoma-Zeiss scale) are in view. The cubic contents of this =  $\frac{1}{100}$  Cmm. Make a mark on the draw-tube—to be used for all occasions. Count twenty fields with above dilution, and add two cyphers to the number so obtained.—B.M.J. i./05,410,576,696,914,1132.

### Leucocytes.—A simple method of counting.

Draw up measured quantity of blood with capillary tube and pipette, and in the same manner ten times as much water. mix on watch glass. Drops (all the same size of the mixture are arranged on a slide (*s.a.*) in line. Dry slowly in the sun or before a fire, then gently agitate in a dish of water until all pigment is washed off. Examined under the microscope each spot will be seen to consist of a faint amount of debris with dark conspicuous leucocytes. They may be stained with Methylene Blue if preferred. Count the cells in several fields, using  $\frac{1}{8}$  in. objective, a stiff paper obturator (pierced with ranks of 20



or more holes made by a large needle—each, on an average with normal blood, to show 2 or 3 leucocytes per hole) is fitted in the eyepiece. If 10 films be searched thus, a good average will be obtained. Two to four fields, each from a different film, is sufficient to count as a rule. The average number per field for normal persons is noted—*i.e.*, 8,000 per cmm. A simple comparison indicates degree of leucocytosis.—B.M.J. ii./09,1749.

A simple method of obtaining a preparation of living, isolated leucocytes.—L. ii./08,1746.

H. C. Ross has devised a method of determining whether leucocytes are living or dead by examining the blood on an agar film containing atropine and a stain.—L. i./09,389. B.M.J. ii./09,514.

**Total and Differential Leucocyte Count** conducted simultaneously.

**Diluent employed** is a mixture of Wright's Modification of Leishman's Stain 4, Acetone 3, Methyl Alcohol 1, Water 12. This is used freshly made up and filtered in any dilution from 1 in 200 to 1 in 10. The white cells stain as in a film, whilst the red are colourless. A dilution 1 in 100 gives about 80 cells on the large square of a Thoma-Zappert Slide which is enough for the total count, whilst 300 elsewhere can be found for the differential. In marked leucopenia, a 1 in 10 dilution gives as many cells as required in a few minutes. In many cases a glance gives the result, *e.g.* a marked eosinophilia, or excess of lymphocytes, large mononuclears or polymorphic cells. The stain is mixed with the blood in a small tube, *e.g.* a Haldane Haemoglobinometer tube cut down to the 120 mark. With this, 24 divisions of water and the rest in proportion are sufficient for a 1 in 100 pipette if it can reach to the bottom.—L. i./12,20.

*Note.*—All tinting solutions should be freshly prepared as precipitates interfere with accurate counting.

The method was found unsatisfactory in hot weather. The following was preferable,—make a  $\frac{2}{3}$  saturated solution of Wright's Stain in Methyl Alcohol by adding 5 Cc. of Methyl Alcohol to 10 Cc. of Saturated Solution. Add 1 part of this to 3 of Saline, 0.1% strength. Stains well without precipitating on the slide.—L. ii./12,1179.

**Leucocytic Extract** in infective processes. It was found that the injection of living leucocytes or their extracts produced remarkable effects upon artificial microbic infections in animals, both for prevention and cure. Latterly the extract has been employed in man. The method of obtaining the extract is to inject sterile 10% suspension of Mellin's Food in Distilled Water in amounts of 5 to 10 Cc., according to size of the rabbit used, into each pleural cavity. The animal is killed 24 hours afterwards and the fluid exudate is removed. Special directions are given to ensure the exudate being removed in a sterile condition,—10 to 20 Cc. is the average amount obtained. The leucocytes are centrifugalised and suspended in an equal volume of distilled water. Finally the 'Extract' is put up in 10 Cc. ampoules and will keep three months. Records of 10 cases treated are provided. The extract seems to act as a marked leucocytic stimulant, *e.g.*, a blood count before injection showed 6,800 leucocytes, 12 hours after injection of 8 Cc.,—the count was 50,000 Again another count gave 5,280 before injection of 3 Cc. After 19 hours the count was 17,000 and so on.—B.M.J. i./11,355.

**A Blood count in a case of medullary leukæmia** showing improvement under Arsenic and Iron.

Red Corpuscles	..	..	3,600,000	after 9 days	4,840,000
Hæmoglobin %	..	..	30	..	45
Color Index	..	..	0.4	..	0.8
Total White Cells	..	..	77,700	..	42,000
Polymorph. Neutrophiles	..	..	50.7	..	46
Large Lymphocytes	..	..	11.2	..	12.5
Small Lymphocytes	..	..	2.3	..	1.5
Hyaline Lymphocytes	..	..	0.5	..	0.5
Transitional	..	..	0.7	..	9.5
Basophiles	..	..	5.5	..	—
Eosinophiles	..	..	0.3	..	4.0
Myelocytes:—					
Neutrophile	..	..	17.0	..	—
Basophile	..	..	11.0	..	26.0
Eosinophile	..	..	0.6	..	—
Mixed	..	..	0.2	..	—

Many nucleated cells, poikilocytosis, anisocytosis, vacuolation.—A. E. Barker, P.R.S.M., Clin. Sectn. March 1910, p. 121.

**MYELOGENOUS LEUKÆMIA** in an infant of 18 months:—

Red Corpuscles 4,080,000 per Cmm., White Corpuscles 63,400, Hæmoglobin 80%, Polymorphonuclears 32·4%, Lymphocytes 5·2%, Large Mononuclears 18·8%, Transitional 12·8%, Eosinophiles 2·8%, Basophiles 0·6%, Myelocytes—Neutrophile 25·8% and Eosinophile 1·6%, Normoblasts 1·6 per 100 leucocytes. The proportion of myelocytes is not so great as is found in cases of this disease in adults. The number of large mononuclears is excessive. It is possible these large mononuclear cells are the precursors of myelocytes, *i.e.*, myelocytes before they have taken on a fine granulation. Myelogenous leukæmia at such an early age is distinctly rare.—P.R.S.M. Diseases of Children, Sect., March 1910, p. 92.

For details of average (adult) spleno-medullary leucocythæmia blood count see Emery, p. 219.

A rapidly fatal case.—B.M.J. i./II, 198.

'X' bodies in the blood in a patient suffering from a recurrent or intermittent urticaria in the Sudan.—L. i./II, 295.

The **TOTAL SOLIDS OF LEUCOCYTES** to extent of 68% consist of Nuclein with 3·01% of Phosphorus. Frick found in the blood of four tuberculous patients an average of 0·291 of Phosphorus, the maximum being 0·351 and the minimum 0·197, whereas in normal blood he found 0·874 parts per 1,000—illustrating deficiency of Phosphorus in tuberculous blood.

**On the Value of Blood Examination to the General Practitioner.** Value of Blood Examination in treatment of chlorosis. Fallacy of giving more iron in one week than the body contains under ordinary circumstances. Chlorosis will improve and recover without any iron at all. In chlorosis the total amount of hæmoglobin is normal even though the readings by the hæmoglobinometer may give figures below normal. A given unit of blood removed from a patient suffering from chlorosis contains less hæmoglobin than the same volume in health—this is due to the fact that in chlorosis the blood plasma is increased in quantity, and there is therefore less room in the particular volume of chlorotic blood for the number of corpuscles usually existant. Though the number of red corpuscles may by a count show as low as 3,222,000, the absolute number of same is really much greater even by as much as three times or more. Therefore, as the total amount of hæmoglobin is normal in chlorosis, each red corpuscle will contain less hæmoglobin than normally.—The investigations of Lorrain Smith.—Batty Shaw; B.M.J. i./07, 973.

Blood examinations in 30 cases of rickets showed that only nine presented anæmia, in not one of which was the number of red cells less than 4,100,000 per c.m.m. In 19 there was a slight increase in the number of white cells.—B.M.J. i./09, 1177.

Cases illustrating the value of an examination of the blood—by blood counts, estimation of hæmoglobin and Serum Tests.—E. H. Shaw, L. ii./12, 286.

**Volume of Blood.**—Method of estimating. The principle employed was to inject into the blood stream a known amount of hæmoglobin, and then determine degree of resulting hæmoglobinæmia.—B.M.J. i./09, 1357.

In **PERNICIOUS ANÆMIA** the red corpuscles, instead of 5,000,000 or more per c.m.m. are only 2,000,000 or even as low as 1,000,000. Hæmoglobin is also reduced, but not to an equal extent. *A very useful account of the microscopy of the blood in this condition.*—B.M.J. i./09 1348.

## Blood Staining.

To make films, prick patient's finger, press, let first drop of blood fall away, place the next drop (small) on the centre of a *really clean*  $\frac{7}{8}$  in. square cover slip. Superpose another and pull off so that the film is thin and even—not 'ridges' and 'valleys' and dry in the air. No fixing is necessary,—the Methyl Alcohol in the stain (Leishman, etc.) does this.

**Jenner's Stain** is used. It may be prepared by mixing freshly 100 Cc. 0·5% Solution of Medicinal Methylene Blue in Absolute



Methylic Alcohol with 125 Cc. of a 0.5 Solution of Eosin (water soluble yellow shade). Filter. A similar stain is produced by dissolving the precipitation compound—(Eosin Blue) in Methyl Alcohol.—*c.f.* Leishman's Stain.

*Method of use.*—Add  $\frac{1}{5}$  volume of Distilled Water to the Stain when on the film (*e.g.* 1 drop to 5 drops), rock gently. Stain for five minutes, then wash in distilled water until pink tint replaces greenish colour. Remove excess of water by filter paper and dry in the air without heating.

Should be kept in stoppered bottles well closed, and is best recently prepared. The Methylene Blue and Eosin are said to combine, forming a chemical compound. In staining it is important to cover with a watch glass to prevent evaporation of the Methyl Alcohol.—*L. i./99* 370.

**Jenner's Stain** is, *we found, improved by using Polychrome Methylene Blue* in place of ordinary Methylene Blue. The 'polychromatising' we effected by adding finely powdered crystalline Sodium Carbonate to the Methylene Blue Solution in the proportion of 1 Gm. of Sodium Carbonate to each 2 Gm. of Methylene Blue. This gave a stain in which blue elements overstained by using Jenner's directions, but by using Wright's method (covering film with a few drops of the Stain, allowing to stand 10 seconds, and diluting with two volumes of water) the resulting film was good.

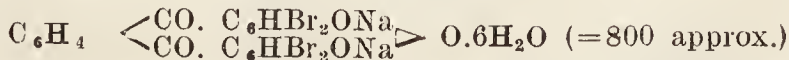
We also found that the proportion of the Eosin Solution may be increased, *e.g.*, Eosin Solution 2 and (*Polychrome*) Methylene Blue Solution 1, gave good result.

**Romanowsky's Stain, Leishman's Modification.**—There are various modes of making and supplying this stain. The following as suggested by Leishman gives the best results (the fixing and staining is done in one process so that fixing by heat is unnecessary):—

This is a solution in pure Methyl Alcohol of an Eosin-Methylene-Blue-precipitation-compound, 0.15 grammes of the compound being dissolved in 100 Cc. of Methyl Alcohol. The solution thus formed is a clear dark blue liquid showing a green iridescence by reflected light. The Stain is used by preparing films of blood in the usual way on clean cover glasses, and allowing to dry in the air. The films should be as thin as possible. Three or four drops of the Stain are dropped on to the film and the cover glass is rotated, no attempt being made to check evaporation as in the case of Jenner's Stain. After about half a minute six or eight drops of water are added, and allowed to mix by rotating with the Stain, and staining is allowed to proceed for five minutes; in certain cases ten minutes may be necessary. The film is now washed with distilled water, and a few drops of the water are allowed to remain on it for one minute. It is finally dried without heating and examined with an oil immersion lens.

(Note, the strength of the Stain may in some cases have to be increased somewhat, the volume of water added in staining may require modifying,—*e.g.*, to the same volume as that of the stain or less.)

Note.—Leishman in his original paper (*B.M.J.* ii./ $\alpha$ 1,757) directs Methylene Blue to Eosin in proportion 10 to 1 to make the precipitation compound. Reckoning water-soluble Eosin as of formula



it may be pointed out that this does not appear to have any relationship with Methylene Blue which has composition  $\text{C}_{12}\text{H}_6\text{N}_3\text{S}(\text{CH}_3)_4\text{Cl}=320$  approx.

1. Mol. Eosin of above formula should be equivalent 2 Mols. Methylene

Blue =  $2 \times 320 = 640$ . In some experiments which we conducted using ordinary Commercial Methylene Blue cryst. 6.4 Gm. ( $= \frac{2 \text{ Mol. Wts.}}{100}$ ) and Eosin (water soluble, yellow shade) 8.0 Gm. ( $= \frac{1 \text{ Mol. Wt.}}{100}$ ) in 1% solutions each; mixing as directed, adding 2.8 Gm. ( $= \frac{1 \text{ Mol. Wt.}}{100}$ ) of Sodium Carbonate cryst. and boiling half an hour, collecting the precipitate and washing until runnings were of pale blue color, we obtained a *better yield* than by Leishman's Method. The precipitate, as above dissolved in the requisite proportion (0.15%) in Methylic Alcohol stained blood films satisfactorily. But even on these lines no chemical formula can be devised to show the reaction. The Stain appears to be based on experimental finding.

The following results are obtained :—

RED BLOOD CORPUSCLES are stained pink or greenish.

POLYMORPHONUCLEAR LEUCOCYTES red. Nuclear network blue. Extra-nuclear protoplasm colourless. Fine eosinophile granules red.

MONONUCLEARS or HYALINE or LARGE LYMPHOCYTES.—Nuclei pale blue. Extra-nuclear protoplasm blue, occasionally showing red granules.

TRANSITIONAL.—As with large mononuclears, except nucleus is reniform.

SMALL LYMPHOCYTES as mononuclears, except nuclei deeper stained.

COARSELY GRANULAR EOSINOPHILES.—Nucleus blue but not so deep Granules pink.

BASOPHILES.—Granules deep-stained purple black. Nucleus red but usually somewhat masked by granules over-laying it.

NUCLEATED RED CELLS.—Nucleus almost black with sharp outline. Extra-nuclear portion grey.

MYELOCYTES stain pale red nuclei pale blue.

BLOOD PLATES deep red with spiky margins, often with pale blue peripheral zone.

BACILLI and MICROCOCCI blue.

MALARIAL PARASITES.—Body stains blue and its chromatin deep red—B.M.J. i./oi,635; ii./oi,757 (with some slight revisions by Wyatt Wingrave embodied).

*Vide* also Malarial Parasites, Vol. I. and this Vol., p. 309.

Wyatt Wingrave finds that the addition of Glycerin (a small proportion) intensifies the Leishman and allied Stains and shortens exposure.

**Leishman's Stain (Wright's Modification).**—Add Methylene Blue 1 Gm. to 100 Cc. of 0.5% Sodium Bicarbonate Solution. Sterilise in a flask in a steam steriliser for one hour. Place in a large dish and add while sterilising, 1 in 1,000 Eosin Solution (yellowish, soluble in water) until the mixture changes to purple and shows yellowish scum on the surface. About 500 Cc. of the Eosin Solution will be required. Collect precipitate formed, and dry in an incubator without washing. When thoroughly dry dissolve 0.3 Gm. of the powder in 100 Cc. pure Methylic Alcohol. Filter this saturated solution and add to the filtrate further 25% of Methyl Alcohol, *i.e.*, to 80 Cc. add 20 Cc. It is now ready for use.

Method of use.—Pour stain on to film and stain one minute. Add water drop by drop until greenish scum forms on surface (for  $\frac{7}{8}$  inch cover glass 6 to 8 drops required), stain with this further two minutes, wash in distilled water, and soak in same 2 minutes or more, until the thinner parts of film appear yellowish pink, dry with filter paper (no heat) and mount in Xylol Balsam.

Normal Erythrocytes appear yellow or pink. In cells deficient in hæmoglobin the colour is from a pale pink with large central clear space to dirty yellow. Polychromatophilic cells bluish. Granular degeneration or basophilic degeneration shows well as small bluish dots in a pink cytoplasm. Normo-blasts have a pink cytoplasm and blue nucleus (in some the cytoplasm is yellowish purplish, or bluish). Megaloblasts show blue nucleus and yellowish or bluish cytoplasm.—M.A. 1906,139.

The various solutions of Eosinote of Blue lose their differential staining power particularly with regard to the granules, after keeping a few weeks (especially in hot weather). Jenner's and Leishman's Stains may be 'reactivated' by adding a very small quantity of the original powder.—Wyatt Wingrave.

**Modified Leishman Stain, using Dibromo-dinitro-fluorescein in place of ordinary Eosin.**

Note.—Dibromo-dinitro Fluorescein has *Syn.* Eosin B. N., Methyl osin (wrongly so-called) and Eosin Scarlet B.



By Romanowsky Staining is meant the production of blue in basophile cytoplasm and violet to magenta in nuclei and some other structures by the stain. Leishman's method though good for parasites is said to give feeble staining of the eosinophile and neutrophile leucocyte granules. The following is said to produce uniform results as regards the blood cells. Add to a filtered solution of Methylene Blue (the strength is immaterial), with stirring, a similar solution of the 'Methyl Eosin' until the mother liquor is only faintly blue,—then add cautiously—often at this stage a weaker solution is desirable—to exactly neutralise. The end reaction is seen by running a drop of the liquid down a sloping glass plate behind which is some white paper—collect precipitate on tough filter paper without pressure, wash with water and dry at not exceeding 50° C. Prepare the stain by dissolving 0.15% of the precipitation compound in pure Methyl Alcohol.

(a) To produce pure blue and pink staining, as distinct from Romanowsky's effect, add 6 drops of the stain to an air dried film. Pour off into 1 Cc. of water in test tube, mix, pour back on to slide spreading with mouth of the inverted test tube. Leave 10 minutes, then wash for a few seconds with distilled water blot to dry.

(b). To produce Romanowsky's staining. If violet nuclei are preferred, use three drops of the Eosin Scarlet Methylene Blue Stain and three of **Eosin Toluidine-Blue** (made similarly but of 0.1% strength).

For staining deeper use 4 drops Eosin-Scarlet Methylene Blue, and 3 drops Eosin-Thionin (0.04%).—Jl. Path. and Bact., July 1911, p. 148.

NOTE.—We have prepared the Eosin Scarlet Methylene Blue using a 1% solution of the Blue, and a 1% solution of the Eosin Scarlet. We found that 110 Cc. of the latter to 100 Cc. of the former was about the correct proportion.

It is not practicable to produce a solution stronger than 0.15% of the precipitation compound in Methyl Alcohol.

An independent report with this stain says—results excellent, quick and reliable,—good for differential counting. Was best employed as follows:—'Flood film for at least three minutes with the stain; dilute with its own volume of distilled water, rock five minutes and wash five times with distilled water.

A method of studying action of blood fluids and other substances on leucocytes.—P.R.S.M. Path. Sect., Jan. 1910, 73.

#### **Wingrave's Simplified Blood Stain.**

Two stock solutions are used:—

I. Methylene Blue saturated solution in 90% (Rectified) Alcohol.

II. Eosin (Water Soluble) saturated aqueous solution.

*Directions.*—Well mix 4 Cc. (about 60 drops) of No. I. with 1 drop of No. II. Flood the film in a Petri dish for three minutes, then add 2 or 3 drops of Distilled Water and stain for 3 to 5 minutes, oscillating constantly, wash well in Distilled Water, then dip into a developer composed of tap water 100 Cc., Glacial Acetic Acid 2 drops, several times quickly and dry with best filter paper. Mop off excess and examine direct. Should Eosin be in excess nuclei will be pale, therefore add more blue. Filtering is not necessary.—Wyatt Wingrave, M.P.C. i./14, 356.

Method of distinguishing dead and living leucocytes by means of Neutral Red. Mix 10 drops of a solution of Sodium Chloride 0.9% containing 0.6% Sodium Citrate with 10 drops of a solution of Sodium Chloride 0.9% containing Neutral Red 0.1%. Add 1 drop of blood or 1 to 4 drops of the sediment of a centrifugalised exudate containing leucocytes. Place in the incubator and maintain at 37° C. for twenty minutes, then count the leucocytes (living stained red and the dead ones not coloured). In circulating blood there are no dead leucocytes even in the most grave diseases. In abscesses the number of dead leucocytes suddenly decreases after an incision. In acute meningitis it appears the variations in the dead leucocytes is valuable for diagnosis; their disappearance is a good sign; increase an unfavourable one;—a few stained nuclei are found in old suppurations, for instance in tuberculous empyema amongst a great deal of leucocytic remains.—B.M.J. ii./10, 1416.

Influence of under feeding on the blood.—Jl. Path. Bact., Oct. 1911.

**Hæmoconia.**—In the intercorpuscular spaces in fresh blood films, made with aseptic precautions, moving bodies are observed of varying shapes ranging in size from a small micrococcus to a small microcyte. F. Porter has classified these into 5 groups and describes changes which take place in such a film during 6 days. See also De Korté and F. C. Eve.—B.M.J. ii./07, 1399.

The phenomenon, which is irrespective of gravity, may be explained by the assumption that the salts in the dried blood cause differences in electrical potential between the different layers of the Agar.—J. S. MacDonald, B.M.J. i./o6,1194.

### **Calcium Salts in Blood, Estimation of by Blair Bell's Calcimeter, v.p 39.**

#### **Methylene Blue Test for Sugar in Blood.**

Mix equal parts of a 1 in 1,000 aqueous solution of Methylene Blue and Liquor Potassæ. To 5 Cc. of this in a test tube add 5 drops of blood from finger, mix and heat gradually in water bath. When sugar is present the blue disappears. Sugar is a normal constituent. We found 0.1 Cc. of 0.5% Glucose will decolorise the blue by this test.

### **Examination of Blood and Urine by determination of the freezing point.**

Lately methods of examination have been introduced to show the excretory power of the kidneys. One important method is the determination of the molecular concentration of the specimen, by a process of "Cryoscopy." The excretory action of the kidney causes different degrees of concentration of the fluid flowing into the kidney as compared with the fluid flowing out of it. Molecular concentration influences osmotic pressure, and is independent of the nature of the substance dissolved in the fluids; it is determined more particularly by the number of molecules dissolved in unit volume: the osmotic pressure of a liquid is proportional to its molecular concentration. We have a very easy way of measuring indirectly the changes in the molecular concentration, and, therefore in the osmotic pressure of a solution by determining the freezing point of the liquid in question. The freezing point of a solution is so much below that of distilled water as its molecular concentration is greater, and *vice versa*. Solutions with the same freezing point have the same molecular concentration, and therefore, the same osmotic pressure.

The apparatus used is the well-known Beckmann's Apparatus, consisting of a thermometer, divided into hundredths of a degree, which is situated in a tube, and in the same test tube there is arranged a stirrer made of platinum wire. The tube is then filled with about 20 to 50 Cc. of the solution to be examined, and is inserted in an outer vessel containing the freezing mixture salt and ice. Gradually the liquid reaches the freezing point—the mercury in the thermometer falls slowly at first, and then quickly until ice formation starts, and at this instant the mercury rises on account of the warmth which is liberated on the formation of the ice. The mercury remains at this higher point for a short time, and this is taken as the freezing point.

Two determinations have to be made—firstly, of the liquid under consideration, and secondly, distilled water. The difference between the two measures the molecular concentration or the osmotic pressure of the liquid. For the purpose of comparison it is obviously necessary to determine the molecular concentration of the blood and of the urine. The value for the blood (which is commonly denominated "delta"), both in the case of man and animals, is fairly constant—namely, about 0.56°; on the other hand, the value for the urine is somewhere about 1 to 2°. It is obvious that any disturbance of the function of the kidneys would make itself evident in these figures—the molecular concentration of the blood would increase, and that of the urine would decrease. A heightening of the molecular concentration of the blood above the normal by the storage up of decomposition products, is very often a valuable sign of insufficient kidney activity—in short, of so-called kidney inefficiency.—From "Pathologie des Harnes," Blumenthal.

Urine testing by Cryoscopy.—B.M.J. i./o6,1063; L. ii./o6,1286.

The objection is the large volume of blood necessary. Sir A. E. Wright's method consists in determining the salt content of a fluid, *e.g.*, urine, by a comparison of the hæmolyzing power of such urine with the hæmolyzing power of varying strengths of decinormal salt solution.—L. ii./o5,1164; i./o7,975.

**Blood Pressure** is determined by some form of the Riva Rocci Sphygmomanometer, *e.g.*, that of Lockhart Mummery.

**Directions** are supplied with the instruments. Another modification of the Riva Rocci Sphygmomanometer is that of C. J. Martin, which is now the leading instrument for the purpose.



**Oliver's Hæmomanometer.**—The latest pattern is a mercurial one and consists of a U tube, which differs from the ordinary form in that it is extended up above the inlet and curves down again to almost meet it. This end may be open or closed to the air and has an indicator for this purpose. When readings not above 200 mm. are required, the right limb is open to the air and the readings on the left are taken. For readings from 200—300 mm. the right limb is closed.

The whole apparatus with stand can be packed together and is unspillable.—Pr. Jan. 1914.

**Barnard & Hill's Instrument.**—B.M.J. i. 07,1253.

The *hæmomanometer* is valuable as giving a record of the contraction and relaxation of the arterial wall rather than of the blood pressure.—L.i./09,451.

**Evolution of Manometers of Stephen Hales, Poiseuille, Ludwig, von Basch, Potain, Gaertner's tonometer, Riva Rocci, and Hill and Barnard's, C. J. Martin's and Oliver's Modification of, Vide L. ii./08,1126 B.M.J. ii./09,64.**

**Sphygmo-Oscillometer (Eckenstein).**—B.M.J. ii./10,1765.

**Pachon's Sphygmo-Oscillometer** gives readings considerably higher than those obtained with the Riva-Rocci apparatus.—B.M.J. ii./11,813,1472.

Two new methods (Auditory and Visual) of reading Arterial Blood Pressure.—P.R.S M., Nov. 19/10, Clin. Sect., p. 8.

#### **BLOOD PRESSURE AND SPECIFIC GRAVITY ESTIMATIONS AS A GUIDE TO TRANSFUSIONS IN CHOLERA.**

A blood pressure of 70 m.m. or less in natives of India (in the case of Europeans it is 80 m.m. or less), indicates a serious degree of collapse. It is necessary to give intravenous injections, but if above these points, Saline injections are readily absorbed when given subcutaneously as hypertonic solutions, or by the rectum as isotonic ones. The estimation of the Sp. Gr. of the blood of even greater value. One employs a series of twelve small bottles of **Glycerin and Water** of each two degrees from 1048, 1050, etc., to 1070. A small drop of blood from the finger is blown gently from a capillary tube into the middle of a bottle, if it sinks it is heavier than the solution, and a higher bottle is tried until it just floats for a few seconds, which is the point required. If it sinks in one and floats in another the point is between the two. The normal Sp. Gr. being about 1056, if it is raised to 1063 or over it is safe to inject intravenously 4 pints in an adult male, and 3½ pints in a female. If the Sp. Gr. be from 1066 to 1070 or over, as much as 5 or 6 pints may be given. The fluid may be run in at the rate of 4 ounces per minute until a full pulse has returned and then more slowly, especially if there is headache or oppression of the chest. It is advisable to dilute the blood to several points below the normal Sp. Gr. so as to allow a reserve of fluid for any further diarrhoea and for excretion through the kidneys so as to remove toxins from the blood. In addition to the intravenous injection, whenever the blood pressure falls to 80 or less in the case of a European, half to one pint of normal Saline solution is also injected high up into the rectum every 2 to 4 hours in all cases to keep the blood fully diluted, and this measure is continued until at least 2 pints of urine are passed in the twenty-four hours.—L. Rogers B.M.J. ii./11,1342; L. ii./11,1403.

**Viscosity of the Blood** is determined by the aid of **Viscosimeter (Du Pre Denning and Watson).**

**Electrical Conductivity of the Blood.**—The 'hæmo-renal salt index' is the ratio of the electrical resistance of the blood to that of the urine. In health the figure would be 3, 4, or 5, thus—

$$\frac{\text{Electrical Resistance of Blood,}}{\text{Electrical Resistance of Urine,}} \text{ e.g., } = \frac{900}{225} = 4.$$

The higher the figure (other things being equal) the healthier the patient.—B.M.J. ii./06,1873.

If the index increases it indicates that the blood contains fewer salts or is richer in corpuscles and that the urine contains more salts and the functional activity of the kidney is increasing. The method is of value in surgical affections of the kidney where one kidney is chiefly affected, where there is a question as to its removal.—B.M.J. ii./08,719; L. ii./08,733.

## Coagulation Time of the Blood.

Sir A. E. Wright's Blood Coagulation Tubes constitute the most accurate method for measuring the coagulability of the blood.

A series of tubes of a standard calibre, 0.25 mm. (approx.  $\frac{1}{100}$  inch), are filled in with blood taken with certain precautions from the finger tip. The coagulability determination is made at a standard temperature, 18.5° C., and the "coagulation-time" is determined by blowing down tube after tube in succession at increasing intervals from the time of filling in.

Normal blood generally has a "coagulation-time" greater than three and less than six minutes.

In many cases, as, for instance, in cases of persons of a "lymphatic" habit of body, and in persons who suffer from chilblains, or urticarias, or spontaneous hæmorrhages, further, in persons who have suffered severely from malarial and other fevers, and pre-eminently in the subjects of hæmophilia, blood coagulation will be found to be very much reduced. Coagulation times of fifteen minutes are not very uncommon in the former classes of cases. In the case of "bleeders," coagulation times of an hour or more are occasionally found.

The following are less exact methods:—

Capillary tubes 6 inches long with internal diameter 1.5 mm. are filled the moment the blood flows from the finger on incision. On breaking the tube (and the column of blood) fibrin formation indicates coagulation point—the time taken is noted, *e.g.*, 7 to 11 minutes in case of the author's blood. The variation in temperature of the room is negligible.—B.M.J. ii./07,1580.

Another method, and simpler, is to drop the blood from a broken capillary tube on to a glass plate. Seal the fractured end of the tube and use the sealed end as a rod to dip from time to time into the drop of blood. Ultimately a fine thread of fibrin will be drawn up—this is the coagulation point; the time can be ascertained to a second.—B.M.J. ii./07,1774. *C.f. also Vol. I. p. 227.*

The value of the estimation is confirmed. There is lessened coagulability in hæmophilia. The prophylactic use of lime salts or serum injections before operations on bleeders is advised.—L. ii./09,34.

## Reaction of the Blood, Determination of.

This method depends on the appearance of a precipitate when a definite amount of Acid is added to a definite amount of diluted blood. A series of small tubes are prepared containing quantities of  $\frac{N}{1000}$ —Sulphuric Acid rising by 0.1 Cc. from 0.0 to 1.2 Cc., the volume in each case being made up to 2 Cc. with Distilled Water. A drop (0.02 Cc.) of blood is then added to each tube, the contents well mixed, and the tube placed in a water-bath at 45° for one hour. With average human blood the tubes containing the smaller amounts of Acid show a slight opalescence, but a coarse, flocculent precipitate makes its appearance when the tubes containing 0.7—0.9 Cc. of Acid are reached. The appearance of this precipitate is considered to indicate the neutralisation point. The reaction is given equally well by fresh defibrinated, oxalated or citrated blood and by red corpuscles washed many times with salt solution. It is not given by citrated or oxalated plasma, by serum or by a solution of fibrin. It is supposed that the precipitate consists of the nucleo-protein of red cells.—J.C.S.A. ii./10,317 ex Arthur E. Boycott and R. A. Chisholm (Bio-Chem. Jl., 1910, 5, 23-31.)

F. Gowland Hopkins deals with the modern views on the Chemical Reaction of the blood and changes which occur.—L. i./14,1589.

**Hæmatoxylin Test Solution.** U.S. 0.2% Hæmatoxylin  $C_{16}H_{14}O_6 + 3H_2O = 356.16$  I. Wts., in alcohol. About 5 drops for a titration. Assumes yellow to orange colour in acid solution and violet to purple in alkaline. The titration is complete when the change in colour remains permanent on adding drop of volumetric solution after stirring.

**Ehrlich - Biondi Stain.** *Syn.* EHRLICH-BIONDI-HEIDENHAIN MIXTURE, EHRLICH'S TRIPLE STAIN.

This nuclear stain is prepared by dissolving separately Methyl Green 1 Gm. in water 200 Cc., Acid Fuchsin 1 Gm. in water 80 Cc., Orange G. 4 gm. in water 400 Cc., and mixing afterwards. The stain is then ready for use; it is *not* to be further diluted. Sections should be allowed to stain from 6 to 24 hours. Dehydration is effected with Alcohol, and the sections are cleared with Xylol,



and mounted in Xylol Balsam. Slides stained 2 to 10 minutes by this process show :—

ERYTHROCYTES, orange. NEUTROPHILE POLYMORPHONUCLEAR GRANULES, violet.

NEUTROPHILE MYELOCYTES, violet. ACIDOPHILE GRANULES OF THE POLYMORPHONUCLEAR CELLS, brick red. BASOPHILES, not stained. LYMPHOCYTES, Nuclei, pale greenish blue. CYTOPLASM, faint pink or grey. In disease the nuclei of the erythroblasts are greenish black. This triple stain should be distinguished from—

### Triacid Stain.

Orange G. saturated aqueous solution 12, Acid Fuchsin saturated aqueous solution 8, Methyl Green saturated aqueous solution 10, water 30, absolute Alcohol 18. Glycerin 5.

The former of these two stains is the more used. The Triacid Stain appears to be more powerful, but is perhaps less delicate.

### Ehrlich's Hæmatoxylin Solution.

Dissolve Hæmatoxylin 1.5 gm. in Alcohol Absolute 100 Cc., and mix the solution with a 100 Cc. of saturated solution of Ammonia Alum in water to which has been added Glacial Acetic Acid 5 Cc. and Glycerin 100 Cc.

**Grenacher's Alum Carmine.** Carmine 1, Alum 5, water 100. A small amount of Phenol may be added to preserve. For nuclei and muscle staining.

### Grenacher's Hæmatoxylin Solution.

Dissolve Ammonia Alum 45 in water 430. Dissolve separately Hæmatoxylin 2.4 in Absolute Alcohol 12. Mix and allow to stand for 14 days. Filter and add Glycerin 66 and Alcohol 90% 75 Cc.

**Delafield's Hæmatoxylin Solution** is similar.

**Borax Carmine.** This solution is prepared by boiling Alcohol 70% with Carmine and Borax in excess, and filtering after cooling.

**Mayer's Stains: Carmalum**—Carmine 2, Alum 5, boil 1 hour with water 100, filter. **Hæmalum**.—Hæmatein [ $C_{16}H_{12}O_6 = 300.096$  I. Wts.] 1, dissolved in alcohol Absolute 50. Mix this solution with one of Alum, 50, in water 1,000. **Acid Hæmalum** consists of the above, with 2% Acetic Acid added. **Hæmatoxylin or Kleinenberg's Hæmatoxylin Solution.** To a saturated 70% Alcohol Solution of Alum and Calcium Chloride, diluted with 6 times the amount of Alcohol of the same strength, is added. Alcoholic Solution of Hæmatoxylin, until the characteristic violet colour is produced. **Paracarmine**.—Carminic Acid 1, Aluminium Chloride 0.5, Calcium Chloride 4 in Alcohol 70% 100. **Picrocarmine**.—Saturated Picric Acid solution is added to a solution of Carmine 8 Gm., in 100 Cc. of Ammonia until a precipitate commences to form.

**Perenyi's Solution** (Hardening Reagent).—Dissolve chromic acid 0.15 Gm. in water 30 Cc. and add alcohol 30 Cc. and nitric acid (10%) 40 Cc. Employed for fixing plant and animal preparations.

## Calculi.

### Urinary Calculi.

A mineral deposit composed of concentric layers of crystallised or amorphous substance cemented together by mucus or other organic material, occurring in the pelvis of the kidney or bladder or urethra. Urinary calculi (sand, gravel or stones according to size) may be classified as follows :—

(1). Those containing a mixture of *Uric Acid with Urates*, with either little or no phosphates; (2). *Mixed calculi*,—those containing more phosphates than Uric Acid; (3). *Calcium Oxalate Calculi*; (4). *Phosphatic Calculi*—composed of Calcium Phosphate. Triple Phosphate or a combination of Calcium and Magnesium Phosphates; (5). *Calcium Carbonate Calculi*; (6). *Cystin Calculi*; (7). *Xanthin Calculi*.—Gould.

### Renal Calculi.

**Chemical composition.**—Calcium is always the base present,—the main acid component may be Oxalate, Phosphate or Urate. The Calcium salt of each of these three Acids is the most insoluble one which exists, this is the reason why it is the invariable one present in renal calculi. It is impossible to associate the 'Mulberry Stone' or 'Jackstone' always with Calcium Oxalate, the 'Pebble' with Urates etc.

The formation of renal calculi 'has for its basis a condition of diminished oxidation in which there appear primarily Calcium Salts of incompletely oxidised bodies such as Calcium Oxalate and Calcium Urate associated with Calcium Phosphate.'

**Method of analysis.**—Determined moisture in the finely powdered stone,—this was found to be 1 to 18% max. in 24 stones examined. Examined qualitatively for  $\text{NH}_3$ , Xanthine, Cystine, Magnesium and Sulphates—these were invariably absent. Calcium was the only base in appreciable amount. Determined the total Nitrogen (usually about 1 to 7% as average). Determined Phosphoric Acid by treating with strong Nitric Acid (destroying all organic matter) precipitated as Ammon-phospho-molybdate, washed free from Acid, dissolved in standard Alkali and titrated back with standard acid.

In another portion (larger) separated Oxalates and Urates by treatment with Hydrochloric Acid (1 in 4), determined Uric Acid by Potassium Permanganate in the insoluble residue, threw down Calcium Oxalate along with Phosphate by adding Ammonium Chloride and  $\text{NH}_3$  to the Acid Solution, filtering into a Gooch crucible, washing thoroughly until Chlorine free, dissolving in Sulphuric Acid and titrating with Permanganate. Results showed with Calculi from kidneys and ureters; Calcium Oxalate mostly about 80 to 99%. Calcium Phosphate either none or up to 40 or even 60%, where Oxalate low. Uric Acid 1 to 10%. Two (from the bladder) out of the 24 Calculi examined were almost pure Uric Acid,—all the others contained Calcium Oxalate,—only one less than 30% and more than  $\frac{2}{3}$  of them over 70% of this salt.—Benjamin Moore, B.M.J., i/11, 739.

**Urethral Calculi** formed *in situ* primarily in the prostate gland and eventually in pockets communicating with the urethra. Examination of encysted calculi in diverticula which communicated with the floor of the prostatic urethra near the neck of the bladder showed in one case Calcium Phosphate 61.5%, Calcium Oxalate 30.8%. Uric Acid 3.9%. *Case 2.*—Calcium Phosphate 94.3%, Uric Acid 1.5%, Calcium Oxalate 2.3%. *Case 3.*—Calcium Phosphate 60.91%, Calcium Oxalate 13.36%, Calcium Carbonate 5.96%. The presence of Calcium Oxalate in a calculus cannot be accepted as evidence that it had descended from the urinary channel above. It has previously been accepted that only phosphatic stones are formed *in situ*, and that urate, uric acid and calcium oxalate stones found in diverticula must have come down the urethra from above.—B.M.J. i/12, 3.

A cystinuric may pass crystals of cystin (*c.f.* p. 234) for years and yet not suffer from cystinuria,—the mere fact of a sparingly soluble substance being present does not necessarily cause formation of a calculus,—the same applies to other varieties of urinary *calculi*,—oxalic, uric and phosphatic alike.—A. E. Garrod, B.M.J. i/11, 1416.

Distilled Water would probably produce results in renal stone far greater than Vittel Water,—the regime and regimen at baths goes a long way.—B.M.J. i/11, 1210.

## Cast.

In the diagnosis of the cause of albuminuria associated with the presence of renal tube casts, it is remarked that owing to improvements in centrifuges, etc., technique has become almost too perfect. Care must, therefore, be taken to distinguish sufficiency of casts to be of pathological significance from 'occasional' casts.

The matrix or groundwork of casts is ~~fa~~<sup>fa</sup> structureless material thought to be due to some kind of protein coagulation. They consist frequently of this matrix alone, and according as they are then less or more highly refractive they are called *Hyaline* or *Waxy* respectively. The Hyaline is the commoner, but neither is characteristic of any particular disease. If renal epithelial cells are embedded in the hyaline matrix, the cast is called an **Epithelial cast**, if leucocytes or pus corpuscles, a **Leucocytic cast**; if red blood corpuscles a **Blood cast**; if bacteria a **Bacterial cast**; if fat globules (degeneration products of renal cells or leucocytes) **Fatty cast**; if non-fatty granular debris **Granular cast**. The cast may be a **mixed** one, *e.g.*, one part hyaline, at one end granular and at the other epithelial. On the whole hyaline casts occur in all forms of nephritic conditions, whether acute or chronic. Epithelial and Leucocyte casts point to active catarrh, Granular ones tend to occur along with Epithelial casts, but when they are alone or in association with Hyaline casts they are evidence of at least less



acute mischief than are Epithelial casts, while Fatty casts come between the two. Blood casts may occur in almost any variety of renal hæmorrhage, though in association with other casts they indicate very acute inflammatory changes.—H. French, B.M.J. i./11,418.

### Cerebro-Spinal Fluid.

In examining a specimen centrifugalize or allow to stand for any sediment to deposit. Examine sediment for cells and Bacteria. Leucocytes indicate an acute process, *e.g.*, septic. Lymphocytes in excess—a chronic process such as tabes; tubercular meningitis, &c.

Red corpuscles when intact indicate hæmorrhage of meninges.

If the fluid be clear, test for Globulin by Salicyl Sulphonic Acid and other Tests (*v. p.* 213) also by Spiegler's Solution, *v.p. ibid* (and Noguchi's test for parasyphilis, p. 322).

Inoculate broth and other media for Bacteria.

Normal cerebro-spinal fluid is clear, colourless, and alkaline; the degree of alkalinity varies. By titration it is shown to be always diminished in infection. It becomes slightly turbid when boiled. The fluid may become coloured. Yellow fluid may indicate tuberculous or chronic meningitis, or tumour of the spinal cord; in subdural hæmorrhage or cerebral laceration it is red, but if the trauma be some days old the colour may be dark amber. Red colour may be due to accidental contamination; coagulation in the test tube is stated to be an infallible sign of this, but such a conclusion is not always justifiable. It has been stated that bile does not appear in the fluid in cases of jaundice; one of the cases described contradicts this. Turbidity is an indication of meningitis, but the fluid may be clear in subacute tuberculous meningitis. It is clear also in extradural hæmorrhage and in cerebral tumour.

A film made from normal cerebro-spinal fluid contains very few leucocytes and many fields may be examined before one corpuscle is found. Absence of leucocytes excludes meningeal inflammation, locomotor ataxy, and superficial gumma of the brain. It does not exclude cerebral abscess unaccompanied by meningitis; this shows the value of making a leucocyte count of the blood at the time the cerebro-spinal fluid is examined.

In pathological states the number of leucocytes is increased, and in inflammatory conditions a varying number of endothelial cells may be seen.

The method of conducting rachicentesis is provided.—James Rae.—B.M.J. i./11,1424. See also Cerebro-Spinal Fever, *Vol. I.*, p. 875; also F. W. Mott,—Cerebro-spinal Fluid—Pathology, properties, chemical alterations, Examination in Sleeping Sickness, Syphilis and Parasyphilis.—L. ii./10,79.

Diplococcus in the blood in cerebro-spinal meningitis, in addition a marked early polynuclear leucocytosis,—early slight cases can be diagnosed by these.—B.M.J. i./12,54.

Method for determining the absolute pressure of the cerebro-spinal fluid.—P.R.S.M. Clin. Section, 1911, 58.

### Noguchi Test for Albumin in Cerebro-Spinal Fluid.

2 Cc. of cerebro-spinal fluid and 5 Cc. of 10% Butyric Acid are boiled together. 1 Cc. N/10 Sodium Hydrate is added and the liquid again boiled when a flocculent precipitate forms. Quantitative estimation of Albumin by modified Noguchi method of the cerebro-spinal fluid.—L. ii./12,685.

Sugar.—The fluid reduces Fehling's Solution. It contains normally 0.4 to 0.5% Glucose. In pyogenic meningitis, pneumococcus, streptococcus and mixed infection Sugar (capable of reducing Fehling) is invariably absent from cerebro-spinal fluid. In cerebro-spinal meningitis sugar is absent in the acute stage but may return in some degree as the infection recedes. In tuberculous meningitis sugar is present except in very rare cases shortly before death, in which stage difficulty of diagnosis rarely exists. In poliomyelitis sugar is present.—F. H. Jacob, B.M.J. ii./12,1097. Test by means of Methylene Blue test as under *Blood*.

### Differential Diagnosis of Syphilitic from the Parasyphilitic affections by examination of cerebro spinal fluid.

Normally the Fluid is practically free from corpuscular elements as stated *antea*—from 1 to 5 lymphocytes may be seen in the centrifugalised deposit in the ordinary microscopic field. In acute microbic infections of the cerebro-spinal meninges as by *staphylococcus*, *pneumococcus*, etc., leucocytosis occurs mostly of the polynuclear type.

In certain more chronic affections as in tubercle, trypanosomiasis and syphilis excess of leucocytes also occurs—mostly *mononuclear*, i.e., there is a lymphocytosis or pleocytosis. Tubercle bacillus and trypanosomes can usually be found, but the *Sp. Pallida* has not been found, in its ordinary form at least. The pleocytosis of cerebro-spinal syphilis, tabes and general paralysis is often a very early occurrence of great diagnostic value.

In florid syphilis and in cerebro-spinal syphilis as well as in tabes and general paralysis, the Wassermann reaction is practically always +.

The second reaction in *diagnosis of parasyphilitic affections* is the finding of an excess of globulin by the Nonne Apelt method :—Mix the cerebro-spinal fluid with Saturated Ammonium Sulphate Solution. Turbidity=excess of Globulin.

This always occurs in tabes, general paralysis and cerebro-spinal syphilis. In combination with a + Wassermann Reaction and pleocytosis it is pathognomonic of parasyphilis.

The third reaction is the pleocytosis ; the fourth, is the Wassermann reaction, both already mentioned. The four reactions are relied upon for diagnosis. At least 95 to 100% of both tabes and general paralysis give a + reaction — using the latest method.—Hauptmann's Auswertung's Method.

Finally the great test is the therapeutical one. In cerebro-spinal syphilis Mercury or '606' in most cases will convert a + reaction to —. In parasyphilitic affections—tabes and general paralysis, this treatment is of no avail.—Sir David Ferrier, L. ii./13,1109.

### Chlorides in Urine.

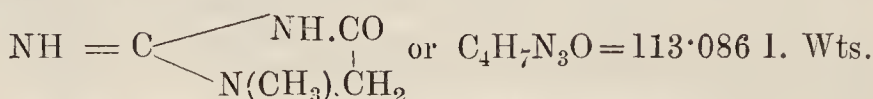
Instead of evaporating and incinerating with ammonium nitrate, oxidise the organic matter contained in 10 to 20 Cc. urine with potassium permanganate, *q.s.*, and sulphuric acid 2 Cc., warm, then neutralise with potash in presence of litmus paper. Dilute to 50 Cc. with water, add potassium chromate and titrate with silver nitrate as usual.—Allen, P.J. ii./04,8.

### Chyluria.

Opacity due to passage of chyle—the milk-white fluid absorbed by the lacteals during digestion. Thought to be caused by disordered condition of the lacteals, and is also connected with presence of filariæ. Note on a case.—L. i./07,733.

### Creatinine.

#### Glycocoll-Methyl. Guanidin.

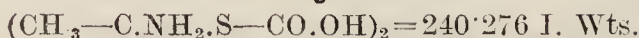


To test for the presence of this body add a little Sodium Nitro-Prusside and Caustic Soda. A red colour develops which fades on boiling the mixture. If a little Acetic Acid be added to the boiling liquid, Prussian Blue is produced.

Retarding effect of Creatinine, Creatine and Mucin on the precipitation of Cuprous Oxide from Fehling's Solution. Urates have auxiliary effect.—L. ii./06,1136 ; ii./07,290.

Excretion of Creatinine in diabetes mellitus.—There appears to be some connection between carbohydrate metabolism and the Creatine-creatinine metabolism. Experiments with diabetic urines showed that Creatinine was not increased to any extent even when patients were on a highly nitrogenous diet. Creatine on the other hand, a substance never found in the normal urine if the diet be free from Creatine and Creatinine was always found, even when patient was on a Creatine-Creatinine-free diet.—B.M.J. ii./10, 1343.

### Cystin.



Cystin is a cleavage product of protein-metabolism, apparently loosely bound and easily split off at an early period of the intestinal digestion. Normally it becomes oxidised and hence is unrecognisable, but in cystinuria it is excreted unchanged.

*Separation of Cystin.* Free from oxalates and phosphates by Ammonia and subsequent addition of Calcium Chloride until this no longer precipitates, add equal volume of Acetone and Acetic Acid in slight excess. Cystin crystal



lises out in 3 or 4 days, and may be purified by dissolving in Ammonia and reprecipitating.—Mann.

Is occasionally found in urinary deposits as transparent six-sided crystals—insoluble in alcohol but soluble with ease in mineral acids, caustic alkalis and ammonia. Uric acid occasionally crystallises in similar form, but gives the murexide reaction; Cystin does not.

Research on some problems of urinary excretion.—L. i./96,674.

Cystin Calculi two cases.—B.M.J. i./97,489.

Garrod on Cystinuria.—L. ii./98,142,214. These lectures should be consulted by those desirous of recent information on the subject.

### Fæces, Examination of.

This is undertaken to determine the state of the various digestive functions, and to assist thereby the treatment of gastric and intestinal disease.

A trial diet is necessary. Various 'meals' have been suggested with the inclusion of Carmine, Carbon, etc., to mark the commencement. The author of this paper advises, however, ordinary meals during 48 hours as follows, to include (1) Milk undiluted or mixed with coffee, (2) Eggs, (3) Animal food such as fish, poultry, veal, beef, etc., (4) farinaceous foods—bread, potatoes, rice, (5) the various green vegetables and roots, (6) stewed fruit, (7) butter and various fats of meat.

The fæces are collected in a glass vessel—this permits macroscopic examination (constipation, etc.).

**Bile, Secretion of.** Stir a portion with concentrated aqueous Perchloride Solution. Normally after some hours all the portions containing *hydrobilirubin* take on a red colour, while those containing *bilirubin* take on green. An indistinct reaction shows that bile secretion is inhibited.

**Fermentation.**—Set aside a portion in a fermenting flask.

Distinct gas evolution in twelve hours shows that **Starch digestion** has not been satisfactory. The fæces in this case are distinctly acid—catarrhal affections of the small intestine. Gas evolution after 24 hours or later shows that the albuminous substances are being split up by the increased alkalinity of the fæces. In the former case there is **intestinal fermentation dyspepsia** and in the latter **intestinal decomposition dyspepsia**.

**Fats.**—All that is necessary is to determine the proportion of *split up* to *total fat*. The splitting up of fats takes place in the small intestine. One determines how much of the total fatty substance present in the fæces appears as *neutral fat*, how much as *soap*, and how much as *fatty acid*. Extract 2 to 3 Gm. in a Soxhlet with Absolute Alcohol, then with Chloroform for six hours. The residue on evaporation contains *all the fats*. Titrate with Alcoholic N<sup>10</sup> KOH. Result: Fatty Acid + Soaps—the triglycerides being calculated as Stearic Acid, the No. of Cc. of Alkali  $\times 0.0284$  gives the amount in Gm. of fatty acid and soaps (Acid Stearic M.W. = 284). The difference between total fat and fatty acid = neutral fat. About 75% of the fats ingested should be split up into soaps and fatty acids and the more the dissociation differs from the normal the greater the amount of neutral fats formed. The average amount of fat taken in health is 125 Gm. *p.d.* This would correspond normally to about 20 Gm. of total fat in the fæces. *The greater the amount of total fat the more defective the fat absorption.*—B.M.J. ii./10,409.

In pancreatic disease the fat content in the fæces is much increased—Hewlett, P.J. i./13,248.

**Blood.**—Benzidin may be used, *e.g.*, make an aqueous extractive filtered about 1=4. To about 2 to 3 Cc. add  $\frac{1}{2}$  Cc. of 10 vol. H<sub>2</sub>O<sub>2</sub> and then add 1 Cc. of 1% Benzidin Solution in 50% Acetic Acid and note blue colouration.

Rub up a piece the size of a walnut with equal volumes of Alcohol and Ether, filter and repeat until a colourless filtrate is obtained, then extract the residue with 4 Cc. of Glacial Acetic Acid and when this has drained off use a further 4 Cc. Shake out the combined filtrate with two or three times its volume of Ether and then with water *q.s.*, to make the separated liquids  $\frac{1}{2}$  Ether layer and  $\frac{1}{2}$  water. Run off the acid aqueous layer, wash the ethereal with water and then treat with 5 to 10 drops freshly made pale yellow Guaia-cum Tincture and 20 drops of Hydrogen Peroxide. In presence of blood a blue to violet colour forms.—Pharm. Zeit., 1913,128; Y.B.P., 1913,43.

**Microscopic Examination.**—The presence of *connective tissue* and *elastic fibres* indicates a defect in acidity of the gastric juice. Defective dissociation of connective tissue and coagulable proteins points to a primary gastric affection known as *achylia gastrica* (Hayem's *hypopepsia*). Appearance of elastic

fibres, if not associated with connective tissue and coagulated protein, must be regarded as a sign of good gastric, but defective intestinal digestion. Considerable amount of undigested muscle fibre with well-marked contour may indicate bad intestinal digestion of meat.

For detection of *B. Tuberculosis* in, by Antiformin, *v.p.* 345.

**Cereal products, Vegetables, etc.,** can be recognised microscopically.

**Starch.**—Lugol's Solution detects. When unchanged and clumped together there is *deficient pancreatic enzyme*. On the other hand, *swollen granules* almost always indicate *catarrhal affection* of the small intestine where the digestion of the starches chiefly takes place.

**Mucus.**—Stain smear with 1% Sodium Alizarin Sulphate. Normal mucus appears as small flakes and scales faintly yellow. It is possible to determine the section of the intestine from which the mucus is derived by the tint of this colour—the further the distance from the anus the mucus has to travel the lighter the colour.—O. Kraus, L. ii./10,95. See also L. i./06,1683.

**Detection of trypsin in the fæces** to assist diagnosis of pancreatic disease. Rub up a small quantity of the fæces with Glycerin, place on a serum plate and incubate at 55° to 60° C. for 24 hours, and note occurrence of depression in the medium. The reaction is not due to Pepsin. The amount of ferment was found to be distinctly greater in loose stools or diarrhœa, indicating that probably owing to the increased peristalsis the reabsorption or destruction of ferment is hindered and an increased quantity voided.—L. i./09,184.

### Formaldehyde in Urine.

We recently had occasion to conduct some examinations on Urine for formaldehyde to determine whether excretion of Formaldehyde occurs after administration of Hexamethylene tetramine and allied bodies. We found the following of service :—

#### Phloroglucin Test.

To 5 or 10 Cc. of sample add 5 drops of 1% Aqueous Solution of Phloroglucin followed by 5 drops of 30% Caustic Soda Solution. Red color appears if formaldehyde present.

Will show 1 in 2,000,000 of Water and 1 in 50,000 of urine.

(Shows no color with Hexamethylenetetramine).

#### Rimini's Test.

To 5 or 6 Cc. of sample add 1 drop of 1% Aqueous Solution of Phenylhydrazine, then 1 drop of 1% Aqueous Solution of Sodium Nitroprusside and 5 drops of 30% Caustic Soda Solution.

Blue color appears if Formaldehyde be present.

Will show 1 in 75,000 of water and 1 in 100,000 of urine.

(Shows no color with Hexamethylenetetramine).

1 in 150,000 of urine can be seen.—J. W. T. Walker, B.M.J. ii./13,654,657.

H. A. B. Dunning provides a colorimetric modification of the Phenylhydrazin Test for Formaldehyde in urine.—Am. Jl. Ph., Oct., 1913.

#### 'Meta' Test (W. H. M.).

To 10 Cc. of sample add 0.05 Cc. of 5% Aqueous Solution of Meta-diamidobenzol Hydrochloride.

Gives a yellow color or precipitate if Formaldehyde present.

Will show 1 in 20,000 of *water* by color and 1 or 2 in 10,000 of *urine* by opalescence or precipitate.

(Gives no reaction with Hexamethylenetetramine).

The 'Meta' Test in conjunction with the others may prove of value in search for Formaldehyde in Formalin poisoning, *e.g.*, with preserved milk or food.

### Glucose Tests.

On the presence of sugar in healthy urine as a source of the Osazone Reaction.—Pavy and Bywaters, with replies by Cammidge :—

The sugar can be isolated from normal urine and confirmed by fermentation test. Directions are given for detecting by Osazone direct in normal urine. *The sugar may amount to as much as 0.25% or more in normal circumstances. The formation of osazone from a*



'suspected' urine is therefore nothing more than a natural occurrence. The Ammonio-Cupric method advised. The reducing power of Creatinine and Uric Acid is a small fraction,—about  $\frac{1}{6}$  of the reducing power ordinarily met with. Difficulty of defining a 'healthy' urine under modern conditions. Sugar is acknowledged to be universally present in the blood, and hence it is argued must also be present in normal urine.—B.M.J. ii./10,78,176,229,296,353.

**Alimentary Glycosuria** occurs when the limit of assimilation for the individual is reached. Breul gave 200 Gm. of grape sugar to a man and examined the urine during the succeeding 4 hours. When at rest he excreted 2.14 Gm., when at work 0.09 Gm.—Mann.

**Phloridzin Glycosuria.** This was first observed by Mering who by giving 1 Gm. of Phloridzin night and morning, produced the daily excretion of nearly 100 Gm. of glucose in the urine. In phloridzin glycosuria there is no increase of glucose in the blood. According to one hypothesis the phloridzin is split up in the kidneys into sugar, and phloretin, *vide ibid.* p. 74 for further consideration of the subject. Also our page 45, and Vol. I. p. 838.

**Renal Glycosuria** is due to an abnormal excretion of the sugar normally present in the blood.

In **pathological glycosuria** the sugar may be formed in the system from other carbohydrates, but also from alimentary and systemic proteins and fats. Much discussion has arisen on this subject. Some claim that sugar cannot be derived from proteins containing no preformed carbohydrate molecule.

Diabetic and non-diabetic glycosuria, *i.e.*, the dangerous disease diabetes in which oxybutyric acid (*q.v.* p. 206) and its derivatives are passed, designated 'composite diabetes' and in which coma may set in; and the relatively harmless alimentary glycosuria have to be distinguished.—B.M.J. i./03,667; L. i./06,676. Significance of small quantities of sugar.—B.M.J. i./06,126.

Glycosuria in tuberculous meningitis. In 15 out of 41 cases glucose was found. It is most apt to appear in the urine during the last days of the patient's life. This variety of glycosuria has its origin in the cerebral lesions and belongs to the nervous group.—A. E. Garrod, L. i./13,15.

**Non-diabetic Glycosuria**, Discussion on, opened by A. E. Garrod.—B.M.J. ii./13,850.

#### DELICACY OF VARIOUS TESTS:—

Fehling's Solution will indicate	..	..	0.0008%
Trommer's	..	..	0.0025%
Nylander's	..	..	0.025%
Fermentation	..	..	0.1 to 0.5%
Phenylhydrazine	..	..	0.025 to 0.05%
Polarimeter	..	..	0.025 to 0.05%

B.M.J. i./07 1472, *q.v.*

#### **Fehling's Solution, Potassio - Cupric Tartrate Solution.**

Glucose being an aldehyde has strong reducing action. In the test the alkaline glucose-cupric oxide when heated causes deposition of the cuprous oxide. 1 molecule of Glucose reduces as nearly as possible 5 molecules of Cupric Oxide.—Mann.

In making use of Fehling's Solution it is important when looking for small quantities of sugar to dilute the urine to about Sp. Gr. 1.015. Mix with an equal volume of Fehling's Solution. Boil for a few seconds.—if no precipitate within two minutes there is no sugar of pathological import. For Life Insurance purposes the Alkaline Safranine test (*q.v.*) deserves to come more into use.—L. i./06,1136, *et seq.*, *vide* also B.M.J. i./07,1471.

The dirty greenish yellow precipitate often formed is probably due to the Cuprous Oxide being in fine granules. Fermentation and other tests should be used in doubtful cases.—B.M.J. ii./12,1280.

Great care, however, should be taken not to confuse with reducing substances other than glucose. Personally we have great faith in Allen's modification of the test, p. 239.

**Fehling's Solution** is prepared in two solutions :—No. 1. Copper Sulphate 34·64, Sulphuric Acid 0·5, Distilled Water to 500.

No. 2. Sodium Hydroxide 77, Sodium Potassium Tartrate 176, Distilled Water to 500.

Mix equal volumes when required. Of this, 10 Cc. will be decolourised and reduced by 0·05 Gm. (or 53 minims =  $\frac{1}{4}$  grain) of glucose or diabetic sugar in solution, with precipitation of yellowish red cuprous oxide when the two are boiled together. No. 2 solution should not be kept in a very cold place or it may crystallise. By keeping the copper solution separate from the alkaline solution the test is prevented from becoming erroneously sensitive.

A little Calcium Carbonate or Barium Sulphate greatly assists the deposition of the cuprous oxide and enables the colour of the supernatant liquor to be more easily seen.

On p. 240 we give a useful Table shewing equivalents in glucose when using **Gerrard-Fehling Solution**. The figures there given apply exactly as if 10 Cc. of 'Fehling's' had been used in place of the Gerrard's Solution.

**Cupric Pellets**,—the salts of Fehling's Solution are prepared compressed into tablets.

**Glass Capsules**, containing about 1 Cc. of Fehling's Solution, are also prepared.

**Glucose \* Endolytic Tubes** are prepared—use similar to those for Albumin *q.v.*

The reaction may be obtained in the cold or by pouring boiling water on to the charged tube (sealing is not necessary). Or, indeed, if not available a lighted vesta drawn carefully along the tube will suffice. If done in the cold, sealed tube to be inspected for usual cuprous oxide precipitate after 12 to 24 hours.

**"Fehling" is reduced** by dextrose, evulose, mannitose, milk sugar, galactose, arabinose, aldehyde, chloral, chloroform, valeraldehyde, resorcinol, pyrogalllic acid, gallotannic acid, trichloroacetic acid, arsenious anhydride, and similar reducing-bodies, glucosides, and acetone, also by

**Glycuronic Acid**  $C_6H_{10}O_7 = 194\cdot01$  I. Wts., Uric Acid, Creatinine, Pyrocatechin, Hydroquinone, Salicylic Acid Compounds; these may be removed by simple repeated filtration through **animal Charcoal**. None of these bodies ferment or give **Osazone Crystals**. *Vide* Phenylhydrazin, p. 239 and 241.

Glycuronic Acid is closely allied to the Pentoses. It conjugates with **phenol indoxyl** and **skatoxyl**, and normally occurs chiefly as phenol-glycuronic acid in combination with potassium.—Mann.

**Creatinin** most markedly of all substances interferes with Fehling's Test—it holds the otherwise precipitable Cuprous Oxide in solution not indirectly by producing Ammonia as Pavy thought.—L. i./o8,85. *C.f.* also B.M.J. i./o7 1472. Creatinin to extent of 3 mgr. per Cc. may be present in normal urine.—L. i./o6,779. *Vide* also B.M.J. ii./12,1280.

**Formaldehyde** being an Aldehyde like Glucose *also reduces*.—should not be used to preserve urines for examination as to diabetes. If in doubt as to presence of Formalin for any reason boil with excess of Strong Ammonia Solution before conducting Fehling's test. Another reason for refraining from its use is that Formalin combines with Urea forming crystals on the side of the container not unlike Leucin.—B.M.J. ii./10,1164,1289,1343.

**Uric Acid** does not introduce any great error by its reduction of Fehling's Solution. Our experiments showed that 1% Uric Acid completely reduced an equal volume of Fehling's with about one minute's boiling. There was a slight reduction with a 0·1% solution with Fehling's, but none with Nylander's



reagent. 10 Cc. Fehling's (=0.05 Gm. of Glucose) by Gerrard's process required 14 Cc. 1% Uric Acid=0.14 Gram which would be equivalent to 250 Cc., Normal urine approximately which would=0.02% +error in estimating Glucose, *i.e.*, the amount is negligible. Consequently Uric Acid does not hinder the reduction of Fehling's Solution by glucose.

**"Fehling" is not reduced** by mannite, dulcitol, sucrose, inositol, cellulose, dextrin, arabin, alcohol, glycerin, phenol, benzaldehyde, salicylaldehyde, acetic lactic, oxalic, succinic, tartaric, citric, gallic, saccharic, mucic, gluconic, actonic, benzoic, salicylic, and sulphurous acids, and alkaloids. —Allen's Urine Analysis.

An orange precipitate formed when hot urine is mixed with hot Fehling's Solution without reboiling, affords almost conclusive evidence of presence of a hexose monosaccharide such as glucose or lævulose.

An orange precipitate formed on boiling is sometimes due to presence of a compound glycuronate. ***To make certain of Glucose the urine must contain a + rotatory reducing substance, fermented by yeast*** (both Glucose and Lævulose are), it must yield ***an Osazone of the correct crystalline form melting at slightly above 200°C*** (both Glucose and Lævulose give) and finally it must yield ***no Osazone*** in case of Glucose ***with Methylphenylhydrazine***, which with Lævulose yields one melting at 150° C.—A. E. Garrod, L. i./12,484.

**Fehling's Test, Allen's modification.**—For small quantities of sugar in urine. Heat 8 Cc. of the urine to boiling point and add 5 Cc. of the copper solution, cool and add 2 Cc. saturated solution of sodium acetate, slightly acidified with acetic acid, to complete precipitation of uric acid, phosphates, and xanthine. Filter, add 5 Cc. of the alkaline solution, and boil for a few seconds. If more than 0.25 per cent. of sugar be present, cuprous oxide is precipitated before boiling point is reached, but if less than this proportion, it is deposited during cooling.—Analyst, xix. 178 ; P.J. ii./95,307.

**Carwardine's Saccharometer** consists of a dropping tube graduated in percentages from 1 to 16. Urine is placed in it up to the mark "U" and diluted with water to a mark "U" (1 to 10 approx.). A volume of Fehling's Solution is measured in a measure provided and diluted with water to approximately double its volume. The diluted Fehling's Solution is then boiled in a test tube and the diluted urine gradually added until the blue colour disappears. The reading coinciding with the level of the urine remaining in the graduated tube gives the percentage.

**Trommer's Test.** To 5 Cc. of urine add  $\frac{1}{2}$  vol. of 15% Sodium Hydrate and then 1 Cc. of 10% Copper Sulphate Solution. A red or yellow precipitate appears in the cold on standing a few hours or more rapidly on boiling. On heating much of the Cupric Hydrate may remain undissolved—an excess of alkali is necessary as in the case of Fehling's Solution (or less Copper Solution can be used). Fehling's Test has superseded Trommer's. They are employed in the same manner. Trommer's Test may be interfered with by Creatinine. H. Maclean points out the importance of adding the Alkali before the Copper Solution.—*c.f.*, B.M.J. ii./12,1280 ; L. ii./12,535.

**Pavy's Ammoniated Cupric Test and Purdy's Test**, which is similar, are now seldom used. For details see Edn. XV., Vol. II., pp. 172,173.

**Barfoed's Reagent.**—Neutral Copper Acetate (*q.v.*) 13·3, Acetic Acid solution (1 per cent.) 200. A Glucose solution warmed with a small quantity of this precipitates Cuprous Oxide.

**Fermentation Test.**—A useful confirmatory test. Prior to conducting, determine the specific gravity of the urine as exactly as possible. Then fill a Doremus tube completely with the specimen; place a little fresh yeast in the bend; keep in a moderately warm position for 24 hours. If sugar be present, carbon dioxide will be produced, and the gravity of the urine will fall—each degree of density lost being equivalent approximately to 1 grain of glucose per ounce. Is stated to be untrustworthy for small quantities.—*L. ii./o6,1136, et seq.*

### Ⓓ Gerrard's Solution.

This is prepared by diluting 100 Cc. mixed Fehling Solution with about 300 Cc. of water and almost decolourising, whilst boiling, with 5% solution of Potassium Cyanide (about 63 Cc. are required), and making up the volume when cold to 500 Cc.

**For the Estimation of Sugar by this Process.**—Mix 50 Cc. of the solution with 10 Cc. of mixed Fehling's Solution (5 Cc. Fehling's No. 1, and 5 Cc. Fehling's No. 2). Boil in a basin and pour into it, whilst boiling, diluted urine,  $\frac{1}{2}$  to 1 Cc. at a time by means of a burette, until the blue colouration just disappears, taking care not to add an excess. An average diabetic urine may be diluted 1 with water to 10.

The calculation is then simple—as in the case of the Fehling method:—

The number of Cc. of actual undiluted urine used contains 0·05 Gm. of Glucose. From this the “percentage”—grammes per 100 Cc.—is easily obtained. To convert this into grains per fl. oz. multiply by 4·375. This product multiplied by 20 gives the number of grains of Glucose per pint. The following table will be found useful:—

Urine diluted 1 with Water to 10.	No. of Cc. of diluted Urine used.	Gm. Sugar per 100 Cc.	Grains per fl. oz.	Grains per pint.	Urine diluted 1 with Water to 2.	No. of Cc. of diluted Urine used.	Gm. Sugar per 100 Cc.	Grains per fl. oz.	Grains per pint.
	4.0	12.5	54.69	1093.80		3.0	3.30	14.45	289.00
	4.5	11.1	48.56	971.20		3.5	2.90	12.70	254.00
	5.0	10.0	43.75	875.00		4.0	2.50	10.95	219.00
	5.5	9.1	39.86	797.20		4.5	2.20	9.64	192.80
	6.0	8.3	36.35	727.00		5.0	2.00	8.76	175.20
	6.5	7.7	33.73	674.60		5.5	1.80	7.88	157.60
	7.0	7.1	31.10	622.00		6.0	1.70	7.45	149.00
	7.5	6.7	29.35	587.00		6.5	1.50	6.57	131.40
	8.0	6.3	27.59	551.80		7.0	1.40	6.13	122.60
	8.5	5.9	25.84	517.80		7.5	1.30	5.69	113.80
	9.0	5.6	24.97	499.40		8.0	1.25	5.49	108.80
	9.5	5.3	23.21	464.20		8.5	1.18	5.17	103.40
	10.0	5.0	21.90	438.00		9.0	1.11	4.86	97.40
	10.5	4.8	21.02	420.40		9.5	1.05	4.60	92.00
	11.0	4.5	19.71	394.20		10.0	1.00	4.38	87.60
11.5	4.3	18.83	376.60	10.5	0.95	4.15	83.00		
12.0	4.2	18.40	368.00	11.0	0.91	3.96	79.20		
12.5	4.0	17.52	350.40	11.5	0.87	3.81	76.20		
13.0	3.8	16.61	332.20	12.0	0.83	3.64	72.80		
13.5	3.7	16.21	325.20	12.5	0.80	3.50	70.00		
14.0	3.6	15.77	314.40	13.0	0.77	3.37	67.40		
14.5	3.4	14.86	297.20	13.5	0.74	3.24	64.80		
				14.0	0.71	3.11	62.20		
				14.5	0.69	3.09	61.80		
				15.0	0.67	3.00	60.00		



The four columns on the right in the table give the results with the urine diluted with an equal volume of water. If the urine contains less sugar than this, it is desirable to use it in an undiluted condition.

The calculation is then as before: the number of Cc. of actual urine used contain 0.05 Gm of Glucose.

#### **Benedict's Modified Fehling Test.**

Copper Sulphate 18 Gm., Sodium Carbonate Cryst. 200 Gm., Sodium Citrate 200 Gm., Potassium Sulphocyanide 125 Gm., 5% Potassium Ferrocyanide Solution 5 Cc., Water to 1 litre. The test is conducted like Fehling's—the end point being disappearance of the blue colour. 25 Cc. = 0.05 Gm. Glucose and 0.053 Gm. Levulose. —B.M.J. ii./12, 1281, 1648. E. F. Harrison's Notes on Benedict's Test, P. J. ii./11, 746.

#### **Gowers' Test, Syn. Moore's Test, for roughly estimating glucose:—**

Dilute with an equal volume of Liquor Potassæ, this makes all urine pale enough to prevent important error in such a rough test. Boil the upper half well but not too long—a lemon tint corresponds to about 5 grains per fluid ounce, a pale sherry to 10 grains, a dark sherry to 15 grains, and a port wine tint to 20 grains and upwards.—*Vide* Brunton on "Diabetes," Reynolds' System of Medicine, Vol. V., 1879, p. 396.

Moore's Test rendered quantitative with coloured Test glasses.—J. C. Parnell, B.M.J. ii./14, 12, 276.

#### **Johnson's Test.**—See Picric Acid, p. 242.

#### **Nitropropid. Sodium Orthonitrophenylpropiolate.**

$C_9H_4Na(NO)_2O_2 = 213.042$  I. Wts.

Has long been used for detection of sugar in diabetic urine. Owing to reduction, indigo blue colour is produced, or indigo-blue itself precipitated. Tablets are prepared. This reaction is based upon Bayer's synthesis of indigo-blue (*q.v.*), which is briefly:—Cinnamic Acid  $\rightarrow$  Orthonitrocinnamic Acid  $\rightarrow$  Dibromo compound of  $\rightarrow$  Orthonitrophenylpropionic Acid, which, warmed with alkali, in the presence of Glucose decomposes thus:— $2C_9H_5(NO_2)O_2 = C_{16}H_{10}N_2O_2$  (Indigo Blue) +  $2CO_2 + O_2$ . This substance is to be distinguished from Sodium phenyl-propiolate (*Syn.* Thermiol). For testing permeability of the kidney with Indigo-carmines *v.* p. 45.

**Solution of Sodium o-Nitrophenylpropiolate** is employed of following composition: Place 5 Gm of o-nitrophenyl-propionic acid in a mortar and wash alternately with 1 to 2 Cc. of water and 1 to 2 Cc. of 10% Sodium Hydrate Solution until dissolved (altogether about 8 to 10 Cc. required). Dilute to 1 litre. On boiling 5 Cc. with 1 Cc. of Urine blue colour of indigo appears either immediately or in  $\frac{1}{2}$  minute according to amount of glucose.—M. '08, 116.

#### **Nylander's Reagent.**

Bismuth Subnitrate 2, Rochelle Salt 4, Sodium Hydroxide Solution (8%) 10; and **Almen's** reagent consisting of Bismuth Subnitrate 1, Rochelle Salt 2, Potassium Hydroxide Solution (35% strength) 50, are used for detecting Glucose. A small quantity of either warmed with the urine will blacken if glucose be present.

This reagent is not interfered with by the presence of Uric Acid. Even a 1% Solution of the acid was found failed to produce any appreciable reduction on boiling 5 minutes.

**Phenyl-hydrazine Hydrochloride.**  $C_6H_5.NH.NH_2.HCl = 144.552$  I. Wts., is used as a test for sugar. It is in colourless, shining, crystalline scales; and should be free from azo-compounds. A small quantity is warmed with twice its weight of sodium acetate in solution, an equal volume of the suspected solution added, and boiled for 20 minutes. On cooling, yellow crystals of phenyl-glucosazone,  $C_6H_{10}O_4(N_2H.C_6H_5)_2 = 358.216$  I. Wts., are deposited if sugar be present.—B.M.J. i./10, 453, 454; L. ii./04, 211, 329, 564.

This substance should be handled with care as it may produce eczema.—Brit. Jl. Dermatology, Aug., 1905.

Boil 2 to 3 Cc. of the urine with equal quantity of water and phenylhydrazine hydrochloride 0.1 Gm. and Sodium Acetate 0.5 Gm. Add 10 Cc. of Sodium Hydrate 10% solution, invert test tube a few times and allow to stand. A pink to red colour of the whole liquid in 5 minutes indicates sugar of clinical significance.—B.M.J. ii./07,19.

(Acetyl-Phenylhydrazin. *Syn.* Pyrocin, Hydracetic. *Dose.*— $\frac{1}{2}$  to 3 grains is antipyretic and analgesic. 10% ointment in parasitic skin diseases.)

**Picric Acid.** JOHNSON'S or BRAUN'S TEST. This has been suggested as a test for Glucose in urine, as a solution of this sugar, if boiled with Picric Acid and Solution of Potash, reduces the yellow Picric Acid to the deep red Picramic Acid,  $C_6H_2(NO_2)_3OH + 9H_2 = C_6H_2(NH_2)_3OH + 6H_2O = 139.102$  I. Wts. forming Potassium Picramate (M.W. 177.194 I. Wts.), the depth of colour depending on the amount of sugar. By the aid of **Johnson's Picro-Saccharometer** this reaction is made a quantitative test.

Solution for use with same: Strong Solution of Ferric Acetate (B.P.'85) 15 drachms, Glacial Acetic Acid  $7\frac{1}{2}$  ounces, Ammonia Solution 0.959,  $3\frac{3}{4}$  ounces. Water to 3 pints.

**Safranine Solution.**—1 in 1,000. One volume of this, with one of urine and one of liquor potassæ is heated to boiling, avoiding agitation. If the urine contain sugar to the extent of 0.1% the liquid will be decolourised. (On cooling colour may return in proportion to the amount of sugar present.) Each additional volume of the safranine solution that may be decolourised represents roughly 0.1% of sugar.—L. i./95,314.

Safranine Solution (unlike Fehling's Solution) is unaffected by Creatin, Creatinine, Uric Acid and Urates. The test deserves to be better known.—L. ii./06,1138. It is only slowly affected by albumin.

*We have had reported to us a lack of success with this test. Personally we find it satisfactory employing the brand of Safranin known as Safrann 'O.'*

For estimation of glucose by polarisation see Mann.

**Alkaptonuria** (rare), due to presence of Di-oxyphenyl-acetic Acid  $C_6H_3(OH)_2CH_2.COOH = 168.064$  I. Wts. Urine reduces Fehling's Solution, and turns brown with alkali. See also Mann *q.v.* also for ochronosis and melanuria.

A case.—L. i./07,660. Of 31 cases of alkaptonuria 15 were in children of first cousin marriages.—Garrod, L. ii./08,5.

Alkaptonuria occurring with pityriasis rubra.—P.R.S.M. Derm. Sect. March, 1910, p. 60.

**Laevulose** reduces Fehling's Solution, ferments with yeast, forms an osazone with Phenylhydrazin like glucosazone. *Vide* also **Crg. Anal. Chart**. Occasionally found in urine alone—more commonly with dextrose. For details of causes, effects and cases see Mann, *q.v.* also for **Lactose**, **Maltose** and **Isomaltose**, and **Heptose**.

## Pentose.

**Bial's Test** (P.G.V.)—Orcin 1 Gm. in 500 Cc. of Concentrated Hydrochloric Acid containing 25 drops of Ferric chloride Solution.

Method of use.—4 Cc. are heated in a test tube to boiling—then add not exceeding 1 Cc. of the specimen. If pentose present, green colour either at once or shortly. Glycuronic Acid does not interfere.—Mann.

For quantities less than 1% the mixture should be heated in a water bath at 96° C. for two minutes, by this means 0.1% or less can be detected (must not be over heated). We found normal urines with these conditions may give a dull olive green colour, therefore one should test a normal urine alongside.

Pentose reduces Fehling's Reagent but is not fermentable. It occurs after excess of fruit such as plums and cherries. Pathologically it occurs in morphia habit.

**NOTE.**—**Orcin.** *Syn.* Methyl Resorcin, Di-*o*-toluol  $1 : 3 : 5$   $C_6H_3(CH_3)_3$ .  $(OH)_2 + H_2O = 142.08$  I. Wts. White crystals turning pink. Very soluble in water and alcohol. Has antiseptic properties but used mostly as test.

**Orcein.**— $C_{23}H_{24}N_2O_7 = 500.212$  I. Wts. Prepared from the above. Reddish powder, soluble in Alcohol with red colour with violet colour in alkalis used as mordant in flagella staining and for demonstrating elastic tissue in sputum.



## Glycerin.

**Glycerin** in the urine is claimed to be indicative of pancreatic disease, and to result from the decomposition of fat. For the method of detection, which depends on the formation of crystals with phenylhydrazin, *vide* L. i./04,783; L. i./05,14. Value of Cammidge's Test questioned. At any rate the urine must be perfectly fresh.—B.M.J. i./06,438. Chronic pancreatitis with notes of examinations of the urine, blood and fæces by Cammidge.—L. ii./05,1824.

Value of Cammidge's Reaction in diagnosis. The characteristic needle-shaped crystals can be obtained from the urine in pancreatitis, acute and chronic. In malignant disease they are found only in about a quarter of the cases, and in these a zone of inflammation probably surrounds the cancerous area.—B.M.J. ii./09,937.

The reaction is one of a number of urine reactions which may accompany alimentary error. Diagnostic power of the reaction not confirmed.—W. Russell, B.M.J. ii./10,5.

Cammidge records results of over 1,500 samples examined. 13 cases (all those examined) of acute pancreatitis gave the test, also in 56% of the cases (204 in number) of chronic pancreatitis associated with gall stone, also in 52% (of 403 cases) of chronic pancreatitis due to secondary disease of the intestine—infection probably of the pancreatic ducts from the duodenum. Analysis of the fæces is also required to gauge the extent and often the nature of the pancreatic mischief and to obtain confirmatory indications as to the cause. Taken in conjunction with clinical symptoms the reaction gives a trustworthy diagnosis of pancreatic disease.—P.J. Cammidge.—B.M.J. ii./10,8. See also chronic pancreatitis with special reference to diagnosis and treatment.—L. i./11,1494.

Cammidge Reaction in 1475 cases (Cammidge).—P.R.S.M. Med. Section 1910, p. 163. See also Path. Sectn., Feb. 1910, p. 79.

## Hippuric Acid.

*Syn.* Benzoyl-glycocoll, *vide* Vol. 1, p. 9.

Hippuric Acid is excreted daily to extent of about 0.5 to 1 Gm. on mixed diet or it may reach 2 or 3 Gm. on vegetarian diet. It is formed by the interaction of dehydrated Benzoic Acid and Glycocoll in the system. Protein in the intestines produces amino-acids which are oxidised to benzoic acid. **Glycocoll** is a normal product of metabolism, and by this reaction renders the benzoic acid (*inter alia*) harmless,—this occurs, it is thought, in the kidneys.

1 of the free acid in 55,000 of water will change Congo red paper to blue, but urine does not cause the change—showing that the Hippuric Acid that is present is in the combined condition.

**Hippuric Acid Estimation.**—Heat 100 Cc. of urine with 10 Gm. Sodium Hydrate in a Kjeldahl flask with reflux condenser 2½ hours. Then add Potassium Permanganate 10 Gm. in small portions and heat gently for 5 to 7 minutes. The liquid remaining at least pink, cool, add small pieces of ice then Sodium Bisulphite 5 Gm. Still keeping the liquid cool add Sulphuric Acid 1:2 *q.s.* to acidify. Shake out five times with Ether. The residue after distilling off the Ether is shaken out with Chloroform. This dissolves out the Benzoic Acid formed. Evaporate and weigh. Multiply resulting acid by 1.468 to obtain quantity of Hippuric Acid.—T. Hryntschak, Y.B.P., 1913, 56.

## Indican.

**Indican**, Potassium Indoxyl Sulphate,  $C_8H_6NSO_4K = 251.228$  I. Wts., may be detected by **Ehrlich's Test**: a Solution of 0.33 Gm. of Dimethyl amidobenzaldehyde in water and strong Hydrochloric Acid of each 50 Cc.

Boil the urine with an equal quantity of this solution. Cool and render alkaline with Ammonia or weak Potash Solution. If Indican be present a red colour results.

**Jaffe's Test.**—Indican may also be detected by adding to the specimen an equal volume of strong Hydrochloric Acid, and adding drop by drop concentrated Liquor Calcis Chlorinata; blue colouration, due to Indigo, if Indican present, which may be taken up by shaking with Chloroform. If shaken with Ether this solvent will dissolve the Indigo-red.





sequently the Nitrogen. The process is recommended for the estimation of various Ammonium Salts.—G. Simpson, P.J. i./14,546.

**Lime Fusion Method of Estimating Nitrogen.** Place 2 Cc. urine and a few Gm. of pure Calcium Oxide in a quartz test tube, connect in a suitable manner with a receiver containing 20 Cc. N/10 Hydrochloric Acid and distil the urine into it until the contents of the test tube are heated to redness. The amount of acid neutralised indicates the amount of Nitrogen present.—M., 1912. This would appear a practicable method.

See also Urea, p. 248.

### Ammonia.

In urine may be estimated by distillation and Nesslerisation of the distillate or by aid of Volumetric Acid, as above.

The average amount of total ammonia in urine is 0.30% by weight.

Ammonia excretion varies during 24 hours—it is greatest during the night. Bodily exercise by producing acids increases output as also does consumption of fat (usually seen after interval of 1 to 2 days).

In fevers, malignant disease, diseases of the liver, ammonia is increased. In pernicious anaemia the amount may be considerably above or it may be rather below the average.

**Malfatti's Method**, using the formation of hexamethylene-tetramin from formaldehyde and ammonium salts, is favoured:—

Add to urine 25 Cc., in a 250 Cc. conical flask, water 50 Cc., and 4 drops of alcoholic phenolphthalein solution 1%. N/10 sodium hydrate solution is added to neutralization, which also gives the amount of acidity. 5 Cc. of 40% Formalin, neutral to phenolphthalein, is added and the titration continued until the pink colour reappears. From the number of Cc. used in the second titration the amount of nitrogen present as ammonia in the twenty hours' urine can be readily calculated. Better colour changes are stated to be obtained if 15 Gm. of potassium oxalate is added to the urine two minutes before titrating. The results obtained by this method are usually somewhat too high.—B.M.J. i./09,715.

It has been pointed out that there is a marked increase in the proportion of Ammonia to total Nitrogen—it may rise from the normal proportion 3 to 5% up to even 45%, of the total Nitrogen—in women suffering from pernicious toxæmia. Vomiting of pregnancy indicates the existence of a serious toxæmia, which, if permitted to continue, will be found to be accompanied by lesions of the liver and other organs, inconsistent with life. A coefficient of 10% according to the author, is a danger signal.—L. ii./05,1172; B.M.J. i./07,316.

In the course of a case of diabetes, late in which disease the diurnal excretion of urea is usually increased, there is a drop in the quantity excreted and a corresponding rise in the ammonia salts, this is an evil omen—probably a warning of acid intoxication and therefore of coma.—L. i./07,784.

**Peptones.** See Albumoses.

### Phosphates in Urine.

(Mean content is 0.15 to 0.2%  $P_2O_5$ .)

These are estimated by means of a **Standard Uranium Nitrate Solution**, prepared by dissolving 35 Gm. of the Nitrate in 900 Cc. of water, and standardising it against 50 Cc. of a solution of 5.042 Gm. of pure Sodium Phosphate (*Off.*) in 1 litre of water 5 Cc. of a solution of Sodium Acetate 100 Gm., with 100 Cc. of Acetic Acid in water *q.s.* to 1 litre is added, both in standardising and in the estimation of the sample of urine. A few small crystals of Potassium Ferrocyanide on a white tile serve as an indicator, the Uranium Nitrate Solution being added to the *hot* Standard Phosphate Solution (or the specimen) until a drop removed by the aid of a rod commences to cause a brownish precipitate with them. This amount of the Uranium Nitrate Solution corresponds to 0.05 Gm.  $P_2O_5$ . The solution may either be diluted so that 10 Cc. shall be equivalent to this quantity (1 Cc. of the Uranium Solution = 0.005 Gm.  $P_2O_5$ ), or better, its strength may be noted and verified from time to time; 50 Cc. of the Urine is the quantity taken for examination, the conditions being the same as above.

Or the Phosphate Solution may be run into the Uranium—the end reaction being clearer, the disappearance of the brown colour is said to be more easily visible than its formation.—P.J. ii./04,9.

**Organically Combined Phosphorus** is in addition present in urine. The daily average is stated to be 11 to 28 mgr. About  $\frac{1}{3}$  of the total ingested Phosphorus is excreted by the bowels.

*Lime* taken in large amount, either apart or in food, causes the Phosphoric Acid in the urine to diminish—(insoluble) Calcium Salts being excreted in the fæces.

The excretion of Phosphoric Acid is increased by the ingestion of small quantities of *Nucleinic Acid*. On a fixed diet for two periods of 8 days the N :  $P_2O_5$  quotient, during one of the periods without Nucleinic Acid was 5.12 to 1, whilst in the other in which Nucleinic Acid was given, the proportion was 3.7 to 1. (The normal is about 5 or 6 to 1.  $P_2O_5$  is not furnished by ordinary proteins but by tissues rich in nuclein.) But administration of (Mineral) Metaphosphoric Acid did not give a  $P_2O_5$  increase in the urine corresponding to the amount given.

In human milk the combined P is 4.15% of the total it contains; in cows' milk it is only 6%. N to  $P_2O_5$  in the former is 3.3 to 1 and in the latter, 2.3 to 1, yet the urine of the child at the breast gave ratio 7 : 1 whilst when fed by hand it was 1.7 : 1, *i.e.*, organically combined phosphorus is retained. Organically combined phosphorus in the urine is probably derived from metabolism of the nuclein containing tissues and not influenced by ingestion of food rich in nuclein—feeding experiments confirm this.—Mann. *q.v.* also for causes of increase and decrease of Phosphoric Acid in the urine in disease.

### Joulie's Ratios.

The so-called alkalinity of the blood is due to the presence of Bicarbonates which are chemically Acid Salts, so that in spite of the alkalinity to litmus the blood may according to Joulie be viewed as an acid fluid. The acidity due to Sodium Acid phosphate is masked by the excess of the Bicarbonates. The blood contains in solution Calcium Phosphate and Magnesium Phosphate, and seeing that these are precipitated in alkaline or even faintly acid solution, this is considered another point in favour of the view that blood is acid in reaction. Bicarbonates are practically absent from the urine. A treatment has been evolved based on determination of the acidity of the urine (according to Joulie, due to Sodium Acid Phosphate) by adding standardised Calcium Saccharate Solution. This acidity shall thence be an index of the acidity of the blood. A precipitate is formed of Tri-Calcium Phosphate which re-dissolves, forming Mono-Calcium Phosphate so long as there is a sufficiency of the Acid Phosphate to combine and produce the soluble Mono-Calcium Phosphate.

Joulie compares the degrees of acidity of urines for equal amounts of Solids in specimens as indicated by the increase in Specific Gravity over that of water, and expresses the result in percentage, *e.g.*, if the Sp. Gr. be 1.015 and we find acidity 0.505 (in terms of  $H_2SO_4$  per litre), then an excess of density equal to 100 would give

$$\frac{0.505 \times 100}{15} = 3.36 \text{ as Ratio of Acidity ('R.A.').}$$

It is then obviously possible to find a Urine with Specific Gravity lower, *e.g.*, 1.005, showing a lower acidity per litre, *e.g.*, 0.308, which is in reality more acid when we eliminate the increase of water—thus

$$\frac{0.308 \times 100}{5} = 6.16 \text{ as Ratio of Acidity.}$$

The determination of acidity per litre is, therefore, considered fallacious. The average R.A. in health is 4.55. A ratio above is hyper-acid, and below is hypo-acid. The latter condition is much more common, due to failure of hepatic function.

In vegetarian diet the excess of alkalis appearing as Carbonates in the urine will produce an alkaline reaction.

To relieve the hypo-acidity with the resultant pathological deposition of lime salts, and the production thereby of phosphatic gout, it is suggested to administer dilute Phosphoric Acid. (Other Acids would have the same effect but they coagulate Albumin and are not well tolerated by the stomach. Phosphorus exists as Calcium Phosphate in the bones, Sodium Phosphate in the plasma, Potassium Phosphate in the nervous system, in combination with Iron in the red blood corpuscles, and as Magnesium Phosphate in the muscles.)

The daily total average loss of Phosphoric Acid is estimated at 3 Gm. in the urine and 1.5 Gm. in the fæces—total 4.5 Gm.



To raise the acidity of the urine (and hence of the blood as Joulie claims) large amounts of Phosphoric Acid have to be given.

Sodium Acid Phosphate would be indicated where there is deficiency of  $\text{H}_3\text{PO}_4$  accompanied by a mild hypo-acidity—usually up to 5 Gm. per diem is given.

**The Ratio of Phosphoric Acid (R.P.)** to excess of density of urine over water is as an average 11 to 11.5. If above this, the condition is called hyper-phosphatia.

Normally  $\frac{\text{R.P.}}{\text{R.A.}} = 2.45$  (Joulie's co-efficient or Acido-phosphoric ratio).

\*Phosphatia, according to Joulie, generally indicates that the R.P. is abnormal. If *excessive*, is treated by diet rich in phosphates—gruyere cheese, haricot beans, mutton, beef, white cheese, eggs, cereals, milk (enumerated in order of preponderating percentages). If R.P. *deficient* this means excessive phosphoric excretion has *preceded*, therefore also administer phosphates; the kind of Phosphate to give depends on the R.A.

If the R.A. is *normal*, a neutral phosphate must be given. **Sodium Sesquiphosphate** as described Vol. I., p. 734, has been suggested and is specially prepared.

Hyper-acidity will rapidly yield to the ordinary Sodium Phosphate, *e.g.*, in the form of Effervescent Sodium Phosphate.—Abstracted from a paper read at the London Homœopathic Hospital, December 5th, 1907, and Jan., 1908. Special Report sheets are arranged, and a table of indications of disease is also prepared. *v. also* L. ii./o6,1382.

The view that the blood is acid is supported. Its alkalinity is only apparent. The carbonates in the serum are certainly present as bicarbonates. Gautrelet appears to have shown that the function of the liver is to correct by acid formation (lactic, etc.), the ammoniacal alkalinity arising from general catabolic changes.—B.M.J. ii./o8,1532.

## Pleural and Peritoneal Fluids, Examination of.

### Physical Characters.

**Colour.**—Note whether blood stained or not. (Caution: A small amount of blood may get into the fluid in the process of exploring.)

Observe whether transparent or otherwise.

Test for fat.

Consistence, Sp. Gr., odour, amount and nature of deposit are stated.

**Chemical Investigation** will give:—

(1) Reaction, (2) Presence of serum albumin and serum globulin, (3) Presence of Mucin or Nucleo-albumin by addition of Acetic Acid, (4) Sugar, (5) Urea for which the fluid must be concentrated to small bulk and all coagulated proteins be removed.

**Microscopic Examination of Sediment.**—For blood, epithelial cells cancer cells, Foulis' cells (these are met with in fluids from malignant ovarian cysts or malignant peritonitis following such cysts), hooklets, crystals, actinomycosis nodules, amœba dysenteriae.

**General Characters.**—It is difficult to tell a dropsical from an inflammatory fluid. It appears that the amount of proteins in an effusion depends much more upon site than upon cause. Pleural fluids contain the highest percentage of proteins, peritoneal fluids rather less and subcutaneous fluids very little. The fluid in cardiac dropsy is more highly albuminous than in dropsy of renal origin. Diagnostically all one can say is that a fluid with Sp. Gr., more than 1.018 containing more than 4% of Albumin is almost certainly inflammatory while one with Sp. Gr., less than 1.015 and an Albumin percentage less than  $2\frac{1}{2}\%$  is certainly dropsical. Fluid obtained by lumbar puncture in cases of cerebral tumour has a Sp. Gr., 1.006 and a Protein content of  $\frac{1}{2}\%$  in chronic cases up to 1 or 2% in acute stages.—For further details see R. Hutchison and H. Rainy "Clinical Methods," 5th Edn., pp. 578–586.

## Purins.

Of the known Purin bodies, Xanthin, Hypoxanthin, Adenin, Guanin, Caffeine, Theobromine, are met with in food, and Uric Acid, Xanthin, and traces of Methylxanthin are found in urine.

\*PHOSPHATIA is applied to a condition of abnormal amount of phosphates and requires the prefix hyper or hypo to indicate excess or deficiency.

They all contain the grouping  $C_5N_4$ —Xanthin is dioxypurin, Uric Acid is trioxypurin. Uric Acid is in the largest proportion of the purins—about 10 to 1 of the others.

There is no special therapeutic effect in a purin-free diet.—B.M.J. ii./07,1759.

Purin in human fæces.—Walker Hall, B.M.J. ii./03,583; i./04,819.

A **purinometer** has been designed for estimating. Full directions are supplied with the apparatus.—L. i./03,899; ii./03,471; B.M.J. i./06,300.

Further directions for using the purinometer, with tables.—B.M.J. i. 06,129.

Solutions for use:—

**SOLUTION No. 1.**—Ammonio-Magnesium Chloride Mixture 100 Cc., Ammonia (20%) 100 Cc., Talc, in fine powder, 10 Gm.

**SOLUTION No. 2.**—Silver Nitrate 1 Gm., Ammonia Solution (strong) 100 Cc., Talc, in fine powder, 5 Gm., Distilled Water 100 Cc.

(Both Solutions require vigorous shaking before use.)

Ammonio-Magnesium Chloride Mixture consists of Magnesium Chloride (crystalline) 110 Gm., Ammonia Solution 250 Gm., Ammonium Chloride 110 Gm., Water 1 litre.

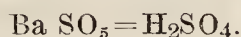
## Pus.

Leucocytes in excess are recognised microscopically—especially on addition of a little acetic acid—this brings into definition the nuclei and at the same times dissolves phosphate precipitates with which a deposit of pus is liable to be confused when the microscopic examination is not conducted.

Leucocytes, Lymphocytes and Plasma cells are stained by employing Pappenheim's Stain.

## Sulphuric Acid.

**Total Sulphuric Acid.**—Dilute 50 Cc. of specimen with equal volume of water, add 10 Cc. HCl. Heat to nearly boiling, add Barium Chloride Solution in excess. Allow to stand on water bath for an hour or two. Collect, wash and weigh.



$$233.44 = 98.086 \text{ (I. Wts.)}.$$

**Ethereal Sulphates.** *Syn. Aromatic Sulphates.* Estimation of—SALKOWSKI'S METHOD.

The ethereal salts in urine are represented by the Potassium Salts of Phenyl-, Indoxyl- and Skatoxyl- Sulphuric Acid and similar derivatives of Catechol and Quinol.—Allen, Chemistry of Urine.

Add to 100 Cc. of specimen an equal volume of a solution composed of Saturated Barium Hydroxide Solution 2 and Saturated Barium Chloride Solution 1, allow to stand a short time and filter. Add HCl in strong excess to 100 Cc. of filtrate (representing 50 Cc. of the specimen). Heat to nearly 100° C. Collect precipitate thrown out, dry and weigh. Multiplied by 0.42 this gives the amount of Sulphuric Acid equivalent to ethereal sulphates. If subtracted from the amount of *total* Sulphuric Acid (*vide* above), the proportion of Inorganic Sulphuric Acid is obtained.

The Ethereal Sulphates normally found represent  $\frac{1}{3}$  of the total sulphates. Partially derived from tissues, the greater part are due to protein decomposition in the intestine—hence their increase in disease brought about by putrefaction and obstruction—or in foul empyemata or gangrene of internal organs.—Pharmacol, p. 56. See also Hewlett, P.J. i./13,248.

In health about  $\frac{1}{10}$  of the Sulphuric Acid of the urine is in the form of aromatic sulphates—aromatic poisons taken with food or formed in the intestines are made to combine with the sulphuric acid which is formed in the system by oxidation of the cystin fraction of proteins. When the intake of or formation of aromatic poisons is excessive the proportion ( $\frac{1}{10}$ ) is higher—in *carboluria* *e.g.*, nearly all the Sulphuric Acid is so combined.—B.M.J. i./11,1415.

## Urea in Urine, Estimation of.

Average 2.5 to 3%, or about (in health) 500 grains (33 Gm.) per diem; it may range between 15 and 40 Gm. The majority of methods are based on the decomposition of Urea into nitrogen, carbon dioxide, and water when treated with sodium hypobromite. The carbon dioxide is absorbed by the excess of alkali present, and the nitrogen can be measured, from which, on reference to tables, the percentage



can be found—theoretically 1 Cc. of nitrogen at  $0^{\circ}$  C. = 0.0027 Gm. approximately of Urea. In the process about 8% of the total nitrogen is suppressed, but the increase in volume of the gas due to the room temperature (taken as  $18^{\circ}$  C.) and the vapour tension (the gas being measured moist) has been found to almost exactly compensate for this loss in practice.

### **Sodium Hypobromite Solution.**

Caustic Soda 100 Gm., Distilled Water 250 Cc. Dissolve, cool, and keep iced while adding *guttatim* Bromine 25 Cc.

Mix and dissolve. This solution is used to estimate the amount of urea in a given quantity of urine. On adding the solution, nitrogen is evolved from the urea and is measured in a **Doremus Tube**, in which each graduation represents 1 per cent. of urea in the urine, or by the ureometer of **Squibb's** pattern, the number of Cc. displaces an equivalent volume of water, and by tables this amount gives the equivalent.

(Sodium Hypochlorite Solution is also used but from a number of experiments which we conducted, we concluded the Hypobromite method is much to be preferred for Urea estimation).

It is better to keep the bromine separate; it may be sealed in tubes containing 1, 2, 3, and 4 Cc. respectively; 1 Cc. of bromine should be added to 11 Cc. of the solution as required. In place of these, **Liquor Bromi**—Bromine 1 Cc., Potassium Bromide 1.5 Gm., Distilled Water *q.s.* to 11 Cc. (= 1 in 11) may be used in equal quantity to the soda solution.

A little Glucose added to a urine increases the evolution by preventing a secondary reaction—formation of Cyanates and Nitrates—but, as indicated above, this is compensated for.—B.M.J. i./03, 194, 288, 341, 403.

Patients treated with Urotropine pass urine which gives an orange precipitate with Bromine water. If due to Albumin, however, does not dissolve on warming.—L. ii./06, 1459.

The **Doremus** form of Ureometer is graduated on the one side in decimal parts of a Gm., of Urea obtained from the 1 Cc. of Urine operated upon, and on the other, the figures 5, 10, 15, and intermediate ones indicate grains of Urea per fluid ounce.

With the **Victoria Ureometer** (an improvement on the old Doremus) no pipette is required, as the urine is added through a tap at the side.

Importance of estimating urea in disease. In renal disease maintenance of normal relation between intake and output of nitrogen is essential. This is far more important than testing for albumin. The gouty patient should have the urea estimated continuously to indicate progress of metabolism. The ordinary person lying in bed will on an average, unless there be some special interference with metabolism, pass urine containing a solution of urea of strength not less than 1.4%.—B.M.J. ii./08, 1498; L. ii./08, 1426.

If there is less urea to excrete the quantity of urine is lessened, not the strength of the solution.

Milroy's Method of Estimation, see B.M.J. ii./12, 791. See also Nitrogen, p. 244.

### **Uric Acid, Syn. Lithic Acid, in Urine, Estimation of.**

$C_5H_4N_4O_3 = 168.072$  I. Wts., when pure is in white crystals, very slightly soluble in water, insoluble in alcohol and ether.

Heated to dryness on a water bath, with a little Nitric Acid or Potassium Chlorate and Hydrochloric Acid in a white dish, cooled, and a little Ammonia solution added gives a red colour.—The **Murexide Reaction**.

Luff expressed the opinion that Uric Acid possesses no toxic properties whatever.—L. ii./05,1864.

(Mean Content 0.05 to 0.06%) **Hopkins' Method.** To 100 Cc. of sample add about 30 Gm. Ammonium Chloride in powder, dissolve as completely as possible, or a small quantity may remain undissolved, add a little ammonia to neutralise and allow to stand 10 minutes. Filter off the precipitated Acid Ammonium Urate, wash with Saturated Ammonium Sulphate solution\* and rinse off the precipitate from the filter with water to 100 Cc. Add 20 Cc. Concentrated Sulphuric Acid to raise temperature of the liquid to about 60° C., or, if necessary, warm to that temp. Titrate with  $N/20$  Potassium Permanganate (158 Gm. in 1 litre), taking as end-reaction the point at which the Permanganate ceases to be instantly decolourised. Each Cc. of the Permanganate Solution = 0.00375 Gm. Uric Acid.

The **Gowland-Hopkins' method** is as above to\*, then proceed as follows:—Wash off the precipitate into a small beaker with a jet of hot water, add a little hydrochloric acid, and heat to just boiling. Allow to stand two hours in the cold. Collect the separated Uric Acid measuring the filtrate at the same time, for which an allowance of 1 mg. must be added on to the final result for every 15 Cc.; it need not exceed 20 to 30 Cc. Wash the uric acid crystals with a little distilled water, rinse off the filter with hot water, warm with sodium carbonate till dissolved and make up with water to 100 Cc. Add 20 Cc. Sulphuric Acid and titrate with Permanganate as above adding slowly towards the end of the reaction, the finish being the first appearance of a pink colour which is permanent for an appreciable interval. Previously the disappearance of the colour is instantaneous.—P.J. i./99,266.

The acid Ammonium Urate may also be decomposed by means of Hypobromite.—L. ii./03,471.

**Uric Acid Outfits** are arranged containing Glass Tubes of Concentrated Permanganate Solution to produce extemporaneously 100 Cc. of  $N/20$  Potassium Permanganate, and the other solutions and apparatus necessary for the entire estimation either by the Hopkins or the Gowland-Hopkins' method.

**Phospho-Tungstic Acid Test** ( $H_3PO_4$  12W  $O_3$  + Aq) for Uric Acid. A rapid approximation.

Mix about 10 Cc. of urine with 3 Cc. of Liquor Potassæ, add 20 drops of Solution of Phospho-Tungstic Acid (20% Solution). Uric Acid causes a blue colour which varies in depth with proportion present. The method is not applicable for anything approaching an accurate colorimetric estimation as the colour fades rapidly. Use a standard for comparison of 1 in 50,000 Uric Acid.

The test can also be conducted by heating the urine with Liq. Potassæ and a 5% solution of Phospho-Tungstic Acid which gives a lilac colour. The intensity can be compared with that given by a Standard Solution of Uric Acid 1—1,000.

**Uricometer.**—A specially graduated tube for the rapid estimation of uric acid in urine. Carbon disulphide is placed in it up to the mark "S" then a solution of "Potassium Iodo Iodide" up to the mark "J" and finally the urine gradually, shaking well after each addition, until the colour of the Carbon Disulphide is a faint pink (almost colourless). Then read off the figure (indicating the quantity of uric acid in parts per thousand) which coincides with the surface of the urine.

The Reagent **Potassium Iodo-iodide** is composed of Potassium Iodide 1.25 Gm., Iodine 0.5 Gm., Alcohol 7.5 Cc., Glycerin 5 Cc., and Water to 100 Cc.

If the urine contains less than 0.25 parts per thousand take half the quantity of Potassium Iodo-iodide and add water to the mark "J," divide the figure obtained finally by 2.

**UROSEMIN.**—A suspension of uric acid in water found to cause a fixation of complement and to produce antibodies which tend to eliminate gout.—Pres., Jan. '13, p. 3.

No relation could be found between amount of Uric Acid and health of rheumatic patients.—J. Heinemann, B.M.J. ii./13,860.

Bread may be a source of Uric Acid by setting free an excess of Phosphoric Acid (0.239 Gm. per 100 Gm. of new bread) an acid which does not find any base that can neutralise it—a case supporting this—Gautier's Opinion.—L. ii./07,87.



Folin and Schaffer's Modified Hopkin's method is said to give satisfactory results.—Z. Phys. Chem., 1901, 32, 552.—P.J. i./14, 60.

### Acidity of Urine.

The **Acidity of Urine**, due mostly to the Sodium Acid Phosphate, is determined by titration with Decinormal Alkali using Phenolphthalein as indicator. Each Cc. of this standard solution = 0.012 Gm. of Sodium Acid Phosphate. Acidity is frequently reported in terms of the number of Cc. of this Alkali per 10 Cc. of Urine, *e.g.*, 3 Cc. = 3°. The **Alkalinity** may be given in similar manner.

The urine of half-a-dozen individuals in health was found by us to have the following 'degrees' of acidity—0.8°, 0.9°, 0.9°, 4.4°, 5.5°, 7.2°.

It was noticeable that this gradation did not correspond with the acidity as shown by delicate litmus paper—on the contrary, the two with 0.9° were distinctly different.

The acidity of the urine, according to Joulie, is dependent on the 'acidity' of the blood (due to acid phosphates). *C.f.*, p. 246.

**Sodium Bi-urate.**  $C_5H_3NaN_4O_3 = 19.0064$  I. Wts. May be prepared by neutralising Uric Acid with Sodium Carbonate. Various opinions as to whether the crystals are the cause or effect of the inflammation in arthritis.—M.P. i./07, 363.

Ratio of Organic Acidity of the urine, *i.e.*, total acidity minus mineral acidity—to total acid increases after injecting Human Tuberculin.—B.M.J. i./13, 214.

A Portable **Urine Test Case** is arranged, containing the apparatus and reagents for the qualitative and approximate quantitative examination of urine for albumin, glucose and urea.—B.M.J. ii./99, 1556; L. ii./99, 1005.

A separate **Urea Apparatus** is also arranged.—C.D. ii./01, 835.

### WATER ANALYSIS NOTES (CHEMICAL).

Work in an atmosphere ammonia-free. The sample of Water should be received in a 'chemically clean' Winchester quart-stoppered bottle, and dated. Note **Physical Characters**, smell, sediment, and colour in a 3 feet tube.

**Total Solids** are ascertained by evaporating 100 Cc. in a platinum crucible on water-bath, the result being expressed in parts per million. The quantity being determined, it is essential that the amount of volatile and non-volatile matter should be determined, or, in other words, the amount of organic and inorganic solids, or those that will disappear on ignition and those that will not. Also notice the appearance on ignition, *i.e.*, charring (indicating organic matter), fuming, scintillation, &c.

**Oxygen absorbed.**—Warm  $\frac{1}{2}$  litre of the sample about 20 minutes in a flask with 1 Gm. Ferrous Ammonium Sulphate  $FeSO_4(NH_4)_2SO_4.6H_2O$  acidified with dilute Sulphuric Acid, then back-titrate with N/10 Potassium Permanganate.

**Free and Albuminoid Ammonia.**—Prepare some water,  $NH_3$  free, by acidulating some good tap water with Sulphuric Acid, about 2 drops of a 1 in 3 solution to a litre of water and distilling. By so doing (the retort and condenser being chemically clean) even the first drop of distillate is Ammonia-free. Distillation may proceed, but must not be pushed too far. The distillate should be Nesslerised to verify its purity. Distil 500 Cc. of sample in a boiling flask with rubber cork to connect with condenser. Nesslerise each 50 Cc. of distillate with standard  $NH_4Cl$  of which 1 Cc. = 0.01 mg.  $NH_3$ . Add together the equivalent quantities of  $NH_3$  and double the result to arrive at number of mgrs. of **Free Ammonia** per litre = parts per million. Stop distilling and add 50 Cc. of a solution of 0.4 Gm. Potassium Permanganate and 10 Gm. Potassium Hydrate which has been freshly boiled 20 minutes. Distil again and Nesslerise the **Albuminoid Ammonia** in 50 Cc. of the distillate at a time until it is  $NH_3$  free. Add the equivalents together and double as above for parts per million.

Wanklyn divides waters in the following:—

*Class I. Of extraordinary purity, yielding from 0.00 to 0.05 part per million of Albuminoid Ammonia, which cannot be objected to organically.*

*Class II. The general drinking waters of this country, containing 0.05 to 0.10 part Albuminoid Ammonia per million—this amount may be considered safe organically.*

*Class III. Dirty waters, yielding more than 0.10 part of Albuminoid Ammonia per million.*

Ⓔ **Nessler's Reagent for Ammonia.** *Syn.* SOLUTION OF POTASSIO-MERCURIC IODOIDE.

Dissolve Potassium Iodide 7 and Mercuric Chloride  $2\frac{1}{2}$ , in Distilled Water 160. To this add more of the Mercuric Chloride in solution until the precipitate no longer disappears on well stirring, and a slight permanent precipitate remains. Then add Sodium Hydroxide 24, dissolve, add a little more solution of Mercuric Chloride and Distilled Water *q.s.* to 200.

On the addition of this test to ammonia or an ammonium salt in solution, it lets fall a brown precipitate which may be Di-mercuric Ammonium Iodide, the equation being



Schmidt gives the composition of the body precipitated as  $\text{HgINH}_2 + \text{HgO}$ —a basic Mercury-Ammonium Iodide.

**Estimation of Ammonia in Water in presence of Hydrogen Sulphide.**

The presence of Hydrogen Sulphide in a water interferes with the Nessler test. If the amount of Ammonia be large the Sulphide may be precipitated with a Zinc or Lead Salt and the Ammonia can then be estimated directly by the Nessler Reagent. If the amount is small it is best to add to 500 Cc. the water, a measured quantity of N of Sulphuric Acid and distil 100 Cc.,—this completely removes  $\text{H}_2\text{S}$ . A volume of  $\text{N}/1$  NaOH equal to that of the  $\text{H}_2\text{SO}_4$  used is now added. The water is again distilled until 200 Cc. have collected and the Nessler test is applied to the distillate.—J.C.S.A. ii./Io, 998.

**Chlorine.** Titrate 100 Cc. in a white basin with standard  $\text{AgNO}_3$  of which 1 Cc.=1 mgr. of Chlorine, using potassium chromate as indicator. The reagents must be Cl-free and the water must not have an acid reaction. The average content is about 2 parts per 100,000, though frequently one finds a content of 5 to 15 parts per 100,000. It should be remembered that urine and sewage are, comparatively speaking, highly charged with chlorine—this enables the analyst to determine whether a high albuminoid Ammonia content is attributable to sewage or vegetable influence. *Per contra* almost entire absence of chlorides, coupled with excess of Albuminoid Ammonia, and little free Ammonia suggests vegetable contamination of a dangerous character. One frequently obtains waters for examination with an exceedingly high Cl-content in conjunction with an almost total absence of organic impurity. Such waters, though 'saline,' are suitable for drinking purposes.

**Nitrites.** To 100 Cc. of the sample add a weak, slightly acidulated, colourless solution of Meta-phenylenediamine. Nitrites give an amber to mahogany colour according to the amount. Conduct a control experiment.

[**Metaphenylene-diamine Hydrochloride.** *Syn.* Lentine  $\text{C}_6\text{H}_4(\text{NH}_2)_2 \cdot \text{HCl}$ . *Dose.*— $\frac{1}{4}$  grain once or several times daily. In acute diarrhœa Adult dose  $1\frac{1}{2}$  grain to 3 grains thrice daily. The urine becomes dark colored.—Gehe, see also Brickdale].

**Nitrates.** The test employed is to mix 1 part of saturated solution of a Brucine Salt with 3 parts of the specimen, and to "layer" beneath this carefully 1 part of pure Sulphuric Solution—a pink colouration indicates their presence.

**Diphenylamine**  $(\text{C}_6\text{H}_5)_2\text{NH}$ =169.098 I. Wts. in 1% solution in sulphuric acid is a very delicate test for nitric acid, giving a blue ring on properly layering.

In the basic condition it is practically insoluble in water and soluble about 1 in 8 of alcohol, 90%.

**Nitrates. Nitric Acid Estimation.**—Treat 100 Gm. of water with two drops of a saturated solution of sodium carbonate, and evaporate to dryness on the water-bath. Treat the residue with 2 Cc. of phenol-sulphonic acid (made by mixing 148 Cc. of pure sulphuric acid, 12 Cc. of water, and 24 Gm. of phenol), add about 25 Cc. of distilled water, and then an excess of ammonium hydroxide. Transfer to a 100 Cc. Nessler jar, make up to 100 Cc. with distilled water, and compare the depth of the yellow colour with that produced by treating different amounts of standard potassium nitrate (containing 0.01 mgrm. of nitrogen as nitrate in each Cc.) in the same manner. If more than



6 parts per million of chlorine are present add to the standards before evaporation an amount of chlorine (in the form of sodium chloride) equivalent to the amount of chlorides present in the sample under examination.

### Phenolsulphonic Acid, Preparation of.

Heat the Sulphuric Acid and Phenol together for eight hours (compare J.C.S.A., 1890, ii., 832) to obtain a reagent which will yield a correct red colour with Nitrates without green.—A. E. Johnson (Chem. News, 1911, 104, 233), J.C.S.A. ii./12,89. Carbonates, *e.g.*, Calcium Carbonate, interfere with the colouration.—Chem. News., Sept. 29/11, p. 160.

**Total Hardness.**—To 100 Cc. of specimen add the least amount of soap solution (standardised so that 1 Cc.=1 mgrm. Calcium Carbonate or its equivalent) that will give a lather which will have an unbroken surface at the end of 5 minutes. 1 Cc. of the soap solution must be deducted from the amount required, as 100 Cc. of Distilled Water would require 1 Cc. to furnish a lather. The number of Cc. of soap solution required gives the number of mgrm. of Calcium Carbonate in the 100 Cc. of the specimen or the parts per 100,000.

**Standard Soap Solution** for the above determination :—Dissolve 10 Gm. of Hard Soap in 1 litre Alcohol 35%. 1 Cc. of this solution will contain soap approximately equivalent to 1 mgr.  $\text{CaCO}_3$ . To standardise to this equivalent dissolve 1 Gm. Powdered Marble or Calcium Carbonate in slight excess of Hydrochloric Acid, evaporate to dryness and redissolve in distilled Water, *q.s.*, to 1 litre. Take, say, 12 Cc. of this solution, add Water to 100 Cc., and then Soap Solution, *q.s.*, to form lather as above. Adjust the Soap Solution until 13 Cc. are required. (100 Cc. of distilled water alone would consume approximately 1 Cc. of the Soap Solution in forming a lather.) We find London tap water varies between 15° and 17°.

**Poisonous Metals.**—Concentrate the water 5 times after acidulating with two drops of Hydrochloric Acid. Add Ammonium Sulphydrate solution. A darkening indicates Pb, Cu, or Fe, but not Zn. This darkened water should be divided into two parts. To one add Hydrochloric Acid—if darkness goes Fe is present. To the other portion add Potassium Cyanide Solution. If darkness goes now the metal is Cu; if it does not, it must be Pb. This latter proceeding is, of course, only necessary when the darkness does not go with Hydrochloric Acid. Confirmatory tests should always be employed. The confirmatory test for Fe and Cu is, to some original concentrated water in a test tube add Hydrochloric Acid and Potassium Ferrocyanide; a blue results with Fe, and a bronze with Cu. For Pb the Potassium Chromate test is employed. Zn gives a white precipitate with Ammonium Sulphydrate, and a white precipitate with Hydrochloric Acid and Potassium Ferrocyanide.

**WELSH WATER.**—A pure soft water acts upon zinc, *e.g.*, on galvanised kettles, in a solvent way, so as to become dangerous to health.—B.M.J. ii./05,1674.

Electrolysis of lead water pipes, owing to leak of 1·8 volts in earthed returns of electric cable, resulting in contamination of the water.—B.M.J. i./06,139.

**EXCESSIVELY PURE WATER** may be solvent of lead in service water. Recommendation to harden it by adding lime.—L. ii./08,1183.

**PEATY WATERS** owing to *acidity* often dissolve lead from main pipes in the form of lead hydrogen carbonate. On standing or on boiling, it is thrown out with the calcium carbonate. Methods of detection and estimation.—P.J. ii./09,663.

**LONDON WATER.**—Houston.—B.M.J. ii./09,85. See also this work, p. 260.

**CHALKY WATER.**—On the influence of calcareous waters in health and disease. Public (and often other) opinion is to the effect that chalky drinking waters may be responsible for a variety of complaints, *e.g.* gout, rheumatism, calculus, constipation, biliousness, dyspepsia, eczema, goitre and arteriosclerosis. For a very useful discussion of this subject see P.G. Lewis. B.M.J. ii./11,158. The author sums up : "There is no evidence that hard water has any bad effect—on the contrary, the evidence is all the other way."

**HARD v. SOFT WATER.**—Tabulated results of examinations give no indication whatever that the hardness or softness of waters have anything to do with the prevalence or mortality from cancer, phthisis or enteric, similarly the character of water supplies in this country has nothing to do with the general death rate.—J. C. Thresh, B.M.J. ii./13,1058.

**LEAD-ABSORPTION** from drinking water, 120 cases.—L. ii./14,213.

In interpreting Water Analysis Reports the bacterial data must go hand-in-hand with the Chemical. In the bacterial the report depends

on the type of bacteria found—the presence of non-pathogenic organisms not necessarily condemning the water.

Before a final judgment can be delivered upon any water there have to be taken into consideration (1) its geological history, (2) the rainfall before and after collection, (3) the method of storage and distribution, (4) the surface drainage, and (5) a bacterial analysis. A water which chemically is organically pure may be bacterially contaminated, and on the other hand a bacterially pure water may be chemically dangerous or suspicious.—Purvis, P.J. ii./10,149.

## WATER.

### Bacteriological Examination.

#### AQUA DESTILLATA.

The following are some recent expressions of opinion as to the bacterial contamination of Distilled Water and the dangers arising from its use. With all due respect to these opinions we are inclined to the view that there has been some exaggeration as to the dangers of the 'dead' bacteria administered in conjunction with 'Salvarsan.'

"*Saline Fever.*" (Fever occurring after saline injection subcutaneously and intravenously). Paul Fildes claims that the fever-producing body in Sterile Saline Solution could be removed by re-distilling the water. "Toxic" Distilled Water was rendered quite "non-toxic" by filtering through a Doulton filter. The toxic symptoms were thought to be due to the (dead) bacteria themselves, *i.e.*, the bacterial protein may be the offending cause.

**Donald's Method** of counting Bacteria in water includes the dead bacteria, whilst the usual cultural methods eliminate them. Extraordinary differences are recorded. A water, for example, grown on Agar two days at 37° C. showed no organisms. On gelatin at 18 to 22° C. 10 to 14 days showed 160—300,000 per Cc., whilst by Donald's method there were 1,500,000 per Cc.

For conducting the method special capillary pipettes made with Bunsen flame are required. These are gauged by means of a standard wire gauge. Drops of the water from pipettes of one calibre are equal in size in certain circumstances. Bacteria contained in the water are counted by evaporating and staining on micro-slides. By the method it was shown that Distilled Water kept for three weeks may develop as many as 15,000,000 of bacteria per Cc.—L. i./13,1447.

Sixteen specimens from various drug stores (*abroad*) were examined, and only two found to contain less than 100,000 germs per Cc.—two having over 700,000 and one 6,050,000. P.G. requires that 100 Cc. on evaporation shall leave not more than 0.001 Gm., *i.e.*, 1 in 100,000 of unknown substances. Suggestion that water should be examined biologically by testing on *Spirogyra*—to test for metallic impurities.—P.J. ii./13,808.

#### **Experiments with Distilled Water.**

It seemed of importance to determine to what extent bacteria may increase in Distilled Water on standing.

500 Cc. of fresh Distilled Water were exposed in a flask and counts made in the usual manner periodically. Examination at the commencement showed *the water to be sterile.*

After 3 days there were 111 organisms per Cc. capable of growth on gelatin [at 18° C.

„ 10	„ „	52,000	„	„	„	„	„
„ 15	„ „	3,800,000	„	„	„	„	„

At this time there was only one organism per 2 Cc. capable of growth on Nutrient Agar at 37° C.

These results show the remarkable contamination in Distilled



Water which may occur by air organisms. Whilst demonstrating the importance of fresh Distilled Water, the relative absence of pathogenic organisms is also of great interest. The cultural method is clearly satisfactory as far as it goes. We have had no personal experience at the time of writing, with Donald's method of counting.

**Ordinary Chemical means** failed to detect any difference in the Water either at the commencement or end of these experiments.

Hort and Penfold state that on adding 1 or 2 Cc. of Distilled Water direct from the condenser drips of a laboratory distilling vessel to Agar tubes will show a large proportion of infected tubes on incubation.—L. i./13,482.

We conducted some experiments on this matter. Five Agar plates were cultivated at about 30° C. with 1 Cc. of Distilled Water collected direct from the worm of a laboratory still. Two of the plates showed about 1,000 colonies each, mostly *Staphylococcus Aureus*, two were covered with *B. Subtilis*. A control plate showed one colony only. Sloped tubes of Agar covered with 1 Cc. of the water in each did not show any apparent growth. The result indicates contamination of the water in the condensing tube from the surrounding air. The water itself, initially, would be sterile.

Drinking Distilled Water, it is said, may be injurious to the system—by osmosis. To drink hard water cannot bring on old age (a fallacy commonly credited).—L. i./13,1813. We doubt this. The same could be said of ordinary water as the difference in osmotic pressure between distilled or ordinary tap water is inappreciable.

**Distilled Water as a Therapeutic Agent.**—Distilled Water injected in dose of 6 to 8 Cc., syphilitic ulcers well treated by—they assumed a healthy appearance after three injections. The theory is that increased surface tension has a good deal to do with beneficial results of injections.—G. Arbour Stephens, L. i./13,799.

C. F. Marshall thinks the effect of Salvarsan may be due, in part at least, to the amount of water injected. Hypodermic injections of ordinary clean water have a therapeutic value by stimulating all the histological structures of the body into renewed activity, causing leucocytosis and increasing phagocytosis.—B.M.J. i./13,794; Pres., May, 1913,172.

## DRINKING WATERS.

### Bacteriological Examination.

**Collection of Sample.**—The apparatus used for collecting the sample is that of V. Esmarch, described by Eyre—Bacteriological Technique, 2nd Edition, 1913, p. 417, or a simple modification of it. Briefly it consists of a sterile bottle which can be opened below the surface of the water,—at any depth by aid of a suspending string. A bottle of capacity 500 Cc. can be used.

If from a water-supply, the water should be allowed to run at least half an hour before collecting; if from a reservoir or stream, surface water must be avoided by holding the bottle at least one foot below the surface.

For comparative purposes it is important to know whether the water, *e.g.*, a well, has been recently disturbed by cleaning out or pumping. Also to examine as quickly as possible after collection of the specimen, particularly in hot weather. To prevent increase in number of bacteria it is customary to pack the bottle in ice for transmission by rail, &c.

Unless the water be packed in ice there is a chance that saprophytic organisms may multiply at the expense of organisms indicative of pollution.

**Enumeration of Bacteria.**—Agar and gelatin plates are prepared with varying quantities of the specimen, *e.g.*, 1·0, 0·1, 0·01 and 0·001 Cc. and incubated at their respective customary temperatures and the colonies counted. A very pure water might of necessity require 3 Cc. The easiest way to do this is to draw sector lines with a paraffin pencil through the petri dish, count one section, and multiply out to obtain the number of bacteria in the entire amount of water taken for examination. **Pakes' Discs** are employed in a similar manner. To obtain accurate results it is important to add the melted gelatin or agar medium to the specimen of water, and not the water to the medium. This procedure ensures better mixing.

The plates are examined daily, and if liquefying organisms are numerous (which suggest sewage pollution) the examination has often to be concluded in a shorter time than would be necessary where such are not present; if possible a week should be devoted to growth.

By cultivation on Gelatin at 20° C., we enumerate the bacteria present normally in the water, whilst the body temperature 37° C. will be more suitable for excremental organisms—derived from, or pathogenic to, the animal body.

As glucose media are very favourable to the growth of many of the yeast and fungi it is advisable also to prepare a plate culture using this medium. Yeast and fungi are therefore often not included in the count with the ordinary media owing to the non-favourable condition for their development. We have proved this with ordinary laboratory tap-water.

J. C. Thresh ('Examination of Waters,' 2nd Edn., 492) says it is desirable to avoid stating that water contains a certain *number of organisms per Cc.*, since such a determination is practically impossible. It is better to state the number of colonies which *grow on a certain medium under specified conditions* of time and temperature and to add whether the colonies were visible to the naked eye or under a certain magnification. He uses nutrient gelatin having a + 1 (acid) reaction.

The next step is to conduct individual search for various sewage polluting organisms, *e.g.*, *B. coli communis*, *B. typhi abdominalis*,—especially the *B. coli* group, *Vibrio cholerae*, *B. proteus*, Klein's *B. enteritidis sporogenes*, and *Streptococci*.

### **B. Coli Communis—MacConkey's Medium.**

The entire problem turns on determining whether pollution with sewage has occurred. For this purpose the detection of the *B. Coli* group of organisms is virtually *the* factor. If we obtain acid and gas production in MacConkey's Litmus Bile Salt Glucose Broth Medium we have presumptive evidence of the presence of *B. Coli*, *B. Paratyphosus*, *B. Enteritidis*—but excluding *B. Typhosus* and the dysentery organisms. These latter produce acid formation only (without gas) in this medium.

Fill ordinary test tubes into which Durham's tubes are introduced, with the following special broth (bile salt broth)—Sodium Taurocholate 0·5, Glucose 0·5, Peptone 2 Gm., Water 100 Cc., with 10 Cc. of 18% Sterile Litmus Solution.

Another step is to employ the MacConkey Medium made with lactose instead of glucose—this forms a useful corroboration for *B. Coli*—this organism gives acid and gas whereas none of the others do so. In tabular form the matter may be stated as follows:—

	GLU- COSE.	LAC- TOSE.	MOTIL- ITY.	GELA- TIN.	LIT- MUS MILK. 3 DAYS.	IN- DOL.
<i>B. Coli Communis</i> .	A.G.	A.G.	+	—	A.C.	+
<i>B. Typhosus</i> ..	A.	—	+	—	A.	—
<i>B. Paratyphosus</i> ..	A.G.	—	+	—	Alk.*	—
<i>B. Enteritidis</i> (Gaertner) ..	A.G.	—	+	—	Alk.	—
<i>B. Dysent. (Shiga)</i> ..	A.	—	—	—	Alk.	—
<i>B. Dysent. (Flexner)</i>	A.	—	—	—	Alk.	+
<i>B. Morgans No. 1</i> ..	A.G.	—	+	—	O	+

A = Acid. G. = Gas. C. = Clot. — under Gelatin means non-liquefaction. \* Vide also Fyfe Bact. Technique, 1913, for *B. Paratyphosus*, A. and B.



The other distinguishing factors in the table are of importance in determining specificity.

The data in question, together with the production of fluorescence in the colonies in **Rebipel Agar**. *Syn.* **McConkey's Neutral Red Bile Salt Agar**—which has the composition:—

Agar and Peptone Witte	..	..	..	..	..	aa. 30 Gm.
Lactose	..	..	..	..	..	15 Gm.
Sodium Taurocholate	..	..	..	..	..	7½ Gm.
Tap Water	..	..	..	..	..	1500 Cc.
Solution of Neutral Red, 1%	..	..	..	..	..	7½ Cc.

constitute the '**Flaginac**' Reaction which is typical of *B. coli*.

This word is made up to show the reactions on these media and is applied to organisms, *e.g.*, *B. Coli*, which will respond to all:—

fl : fluorescence in neutral red.

ag : acid and gas formation.

in : indol in peptone water.

ac : acid and clot in Litmus milk.

**Neutral Red** (*Syn.* Toluylene Red) is chemically Dimethyl-diamido-toluphenazine hydrochloride.

The exact mode of procedure which we employ for the detection of Acid and Gas formation is as follows:—

**First for Examination of 100 Cc. of the Water** we place 50 Cc. of **Triple Strength of McConkey's Broth Medium made with Glucose** into a 150 Cc. bottle (an ordinary strong green flint bottle is suitable), containing a small inverted test tube, rendered bubble free *secundum artem*. The whole is then plugged with Sterilised Wool and sterilised on three succeeding days in the usual manner. This has to be made ready before receipt of the specimen. 100 Cc. of the sample to be examined is introduced with aseptic precautions.

The same procedure is gone through with the *Lactose* preparation. These are then incubated 24 hours.

**For the Examination of 50 Cc. of the Water** we take 50 Cc. of **Double Strength** McConkey's Medium made with Glucose and Lactose respectively and 50 Cc. of the specimen in a 100 Cc. bottle, and incubate as before.

**For Examining 10 Cc. of the Water** we take 10 Cc. each of the Double Strength Media and 10 Cc. of the sample and proceed on exactly the same lines.

Subsequent to these results we inoculate Neutral Red Bile Salt Agar Plates with loopfuls from the cultures in the bottles—using a 'spreader' made with a piece of glass rod  $\frac{1}{8}$  inch diameter with a bent end about 1½ inches long at right angles to the handle.

After incubating 24 hours pick out with a platinum loop Colonies resembling those of *B. Coli*, and inoculate Sloped Agar tubes, *thence* Peptone Water for the Rosindol Reaction and Indol Reaction—also Litmus Milk for the 'Acid and Curd,' and examine a fresh broth culture for motility.

The plate cultures are incubated further to observe fluorescence, if any.

**Rosindol Reaction** (Ehrlich's). *Syn.* Böhme's Indol Test.—To 10 Cc. of a 48 hour Peptone Water culture add 5 Cc. of the following solution:—

Paradimethyl-amido-benzaldehyde	..	..	..	..	1
Alcohol, 96%	..	..	..	..	95
Concentrated Hydrochloric Acid	..	..	..	..	20

and then 5 Cc. of Saturated Aqueous Potassium Persulphate Solution. Shake well. McConkey says 1 Cc. of each solution is sufficient, and we have found it so. Pink colour in a few minutes = +. In some cases the Persulphate need not be added. The pink colour is soluble in Amyl Alcohol—a little of which should be added, especially in doubtful cases. At least 48 hours growth should be allowed, in some cases 6 to 8 days are required.

**Indol Reaction.**—To 5 Cc. of the (6 or 7 days) Peptone Water culture add 1 Cc. of Concentrated Suphuric Acid and then 1 Cc. of 0.02% Sodium Nitrite. Pink colour indicates Indol production (some organisms, *e.g.*, cholera vibrio do not require the Sodium Nitrite—hence the test may be done in two stages). It may be necessary to incubate for 8 days or more before conducting the test.

Our own experience with these two reactions is disappointing—on the whole we think the Rosindol Reaction is the more conclusive (*c.f.* also *B. Coli* in Urine, p. 293).

The formation of Indol amongst the 'flaginac' characters of *B. Coli* is the character most liable to be absent in *B. Coli* isolated from urine (and water). The Rosindol Test preferred.—A. R. Tankard, P.J. i./13,126.

Thresh gives the following as "decisive tests" for *B. Coli*. (1) Acid and Curd in Litmus Milk (2 and 3), Motility and Indol in Peptone Water. (4) Negative to Gram's stain. (5) Liquefaction with streak cultures on gelatin. (6) Fluorescence on Rehipelagar (7, 8 and 9). Fermentation of Sucrose, Mannite and Dulcitol respectively.—(Examination of Water Supplies, 2nd Edition).

Gaertner deals with the difficulties of examining water for this organism. A thorough investigation of the source and history of a water under examination is necessary,—this is more important than laboratory diagnosis. To ascertain the origin of the organism if found,—whether from sewage or other human source, cattle, cultivated lands, etc.—B.M.J. i/11,1334.

Sodium Salicylate 0.25% is said to inhibit growth of *B. Typhosus*. In Nutrient Broth even 0.2% will do so. Useful for demonstrating *B. Coli* in sewage polluted water. The only organism likely to grow with *B. Coli* is *B. Subtilis*, which can be separated by plating and tested by sugar fermentation.—L. ii./12,439; P.J. ii./12,270.

**B. Typhosus.**—In searching for this organism, which is a very difficult matter, and almost invariably attended with negative result, the enrichment method of Hoffman and Ficker is recommended side by side with some method of chemical precipitation. Nowadays it is the custom to accept the indirect bacteriological evidence obtained by the *coli-form* data, as sufficient for the purpose of condemning or passing a water for drinking purposes. Scheme of work for isolating *B. Typhosus*:—

- |  |  |  |  |                           |
|--|--|--|--|---------------------------|
|  | 1. Chemical precipitation—Schüder's or Ficker's process.   |  |  |                           |
|  | 2. Serum agglutination.  |  |  |                           |
| 1. ISOLATION.                                      | 3. Caffeine enrichment process.  |  |  |                           |
|  | 4. Solid Media { <table border="0" style="display: inline-table; vertical-align: middle;"> <tr><td>Rebipel Agar.</td></tr> <tr><td>Glucose and Lactose Agars.</td></tr> <tr><td>Drigalski-Conradi Medium.</td></tr> </table> | Rebipel Agar.                              | Glucose and Lactose Agars.                         | Drigalski-Conradi Medium. |
| Rebipel Agar.                                      |  |  |  |                           |
| Glucose and Lactose Agars.                         |  |  |  |                           |
| Drigalski-Conradi Medium.                          |  |  |  |                           |
| 2. IDENTIFICATION.                                 | { <table border="0" style="display: inline-table; vertical-align: middle;"> <tr><td>Morphological and cultural characters, &amp;c.</td></tr> <tr><td>Specific Reactions: Pfeiffer's Agglutination Test.</td></tr> </table>   | Morphological and cultural characters, &c. | Specific Reactions: Pfeiffer's Agglutination Test. |                           |
| Morphological and cultural characters, &c.         |  |  |  |                           |
| Specific Reactions: Pfeiffer's Agglutination Test. |  |  |  |                           |

**Schüder's Process** consists in adding to 2 litres of the water 20 Cc. of 7.75% Solution of Sodium Hyposulphite and 20 Cc. of 10% Lead Nitrate Solution. Plates are made from the precipitate containing the bacilli.

**Ficker's Process.**—Render 2 litres faintly alkaline with Soda and add 7 Cc. of 10% Ferrous Sulphate Solution. The precipitate is dissolved in 25% neutral Potassium Tartrate, and plates are prepared.

**Serum Agglutination.**—Add 1 Cc. of the sample to each of a number of broth tubes, and incubate at 37° C. three or four days. To those with sediment add a few drops of active anti-typhoid serum. Clumps are centrifuged, and the clear liquid drawn off. Emulsify deposit and prepare plates.

**Caffeine Enrichment process.**—To the sample add Nutrose (a proprietary Sodium Caseinate) 1%, Caffeine 0.5%, Crystal Violet 0.001%. Incubate 12 hours at 37° C. Isolate typhoid bacilli on plates,—the colon bacilli will have been almost entirely restrained in their growth; the method is, however, not wholly reliable.

**Solid Media.**—**Drigalski-Conradi Medium** consists of a nutrose-lactose-litmus agar containing 1% Nutrose, 1% Peptone, 0.5% Salt, 3% Agar, 1.5% Lactose, in a nutrient broth made with 750 Gm. Horse Flesh to the litre, also 13% of Kübel and Tiemann's Litmus Solution and a trace (0.001%) of Crystal Violet. After incubation typhoid colonies are blue, glassy-like dew drops, Paratyphoid similar, and *B. Coli* are bright red and opaque. See also Abel & Gordon's Handbook, and J.I. Hygiene, Oct., 1905.

**Rapid method which may be utilised in search for *B. typhosus*.**—"Concentrate" at least two litres of the water by filtration through a Cham-



berland filter. Brush off the organisms from surface of candle into sterile vessel containing about 10 Cc. of sterile water. Brush plates with the emulsion and cultivate in the ordinary manner on gelatin and agar, with the addition of phenol 0.05%. This addition inhibits many common water bacteria, but not *B. Typhosus* or *B. Coli*. After incubation suspicious colonies are picked out and cultivated on various media, concluding with the serum diagnosis method of Pfeiffer.

**Vibrio Cholerae.**—To detect: inoculate peptone water, preferably in an Erlenmeyer flask with 100 Cc. of the water. Incubate and test for indol production and search for typical comma-shaped organisms, which are actively motile and decolourised by Gram's method. Test further with usual laboratory media, and also conduct serum agglutination test.

The above method somewhat modified used for cultivation. For identification are motility, Cholera Red Reaction, Nitroso Indol, Ehrlich's Rosindol Reaction, Flagella staining, and Agglutination Test. Possibilities of carriers.—L. i./13,1377.

**B. Proteus.**—The ordinary laboratory media and methods may be employed for the various types of *Proteus*.

**Bacillus Enteritidis Sporogenes.**—Eyre (Bact. Technique, 1913) states, this bacterium is relatively scarce in water and the search for it is not usually included in the routine examination. Add to a fresh milk tube 1 Cc. of the water or a small quantity of the 'concentrated' water. Heat to 80° C. for 20 minutes to kill off other organisms, excepting spores of the organism searched for (Kitasato's method); grow in Buchner's tube, i.e., in an atmosphere of nitrogen for 24 to 36 hours. If result be separation of milk, stringy curd, and excessive whey, test for pathogenicity on guinea-pig. The animal succumbs within 36 to 48 hours (if very virulent in 24). Post-mortem signs: bloody œdema at seat of inoculation, offensive odour, hair of animal easily detached. Films stained by Gram's method from œdema fluid show typical non-sporing organisms. To further test, a blood serum tube is inoculated from the œdema fluid and incubated under anaerobic conditions. The medium is eventually liquefied by the organism and films prepared from this show the typical sporing organism of Klein.

**Streptococci.**—Eyre (Bact. Technique, 1913) states the Streptococci are frequently termed 'microbes of indication,' as their presence is held to be evidence of pollution of water by material from the mammalian alimentary canal—thus constituting a danger signal. Glycerin Agar is a good medium for this organism. Agar plates may be brushed or prepared in the ordinary way, incubated at blood heat, and all discrete colonies examined by films or ordinary sub-cultures made on various laboratory media.

## DRAWING UP BACTERIOLOGICAL REPORTS ON WATERS.

If *B. Coli* form a considerable proportion of the total number of organisms present there is great reason to suspect sewage pollution.

It must also be remembered that *B. Coli* may be of human intestinal origin or a natural inhabitant of the water. Muir and Ritchie, for example, mention a moorland water with high *B. Coli* content—certainly *not* of human origin—hence it is of importance if possible to examine the nature of the surroundings.

The following is a brief résumé of the customary standards:

*A water generally speaking containing B. Coli in 50 Cc. but not in less is quite good if the count of total bacteria and chemical result are good. See also filtered London Lea River Water p. 260.*

### Wells, Shallow and Surface.—

If chemical results and surroundings are bad, even if *B. Coli* be absent from a large volume of the water, it should be condemned,

and *per contra* if in a suspicious locality the bacteriological examination is bad the water ought to be condemned even though chemically it could be passed.—M. and R.

### **Wells, Ordinary or Medium Depth.—**

**Total Bacteria.**—The Gelatin Count may show from 100 to 2,000 organisms per Cc. The presence of *B. Coli* in 10 Cc. would condemn the water.

### **Wells, Deep.—**

**Total Bacteria.**—Should not exceed 100 bacteria per Cc. Artesian Wells and some springs may contain very small amounts, e.g., 5 or 10 organisms per 100 Cc.

Presence of *B. Coli* in 100 Cc. or less cannot be permitted.

**Rivers.**—Draw conclusions as under Wells (Shallow). Content varies enormously with season.

**Total Bacteria.**—The Gelatin count varies enormously. *B. Coli* in 10 Cc. would condemn.

### **Town Supplies (Filtered).—**

**Total Bacteria.**—Should not show more than 100 Bacteria per Cc.—Muir and Ritchie.

For *B. Coli c.f.*, Lea River Water *infra*.

### **London (Lea River filtered).—**

Though *B. Coli* in one series of examinations was present in 93% of samples in 1 Cc. or less before filtering it was absent from 100 Cc. in 62% of samples after filtering, and therefore present in 38% in 100 Cc.—Houston.

A well known authority on Bacteriological Examinations of Water informs us that he would expect ('exceedingly likely') *B. Coli* in 100 Cc. main tap water in London.

A further report (1912) resembles previous ones in being favourable. Dealing with *B. Coli*, taking one figure results, this organism occurs in raw Thames water to the extent of 19 organisms per Cc., Lea water 5 organisms, New River 2 organisms. For *filtered* waters a one figure result per Cc. of water—expressed as typical *B. Coli* per 1,000 Cc., gives Kent 1 to 2, West Middlesex 14, New River 2 to 3.—A. C. Houston, B.M.J. ii./12,1671.

Raw Thames water in 1912-1913 contained 6,550 microbes per Cc., Lea water 11,772, New River 2,777. On filtering the figures were respectively 14.5, 30.5, and 12.6—indicating a percentage reduction of 99.8, 99.7, and 99.5. Too much stress, however, must not be laid on percentage reduction. The worse a water is initially the easier it is to obtain a big percentage reduction.—A. C. Houston, B.M.J. ii./13,678. This authority has recently issued a monograph, 'Studies in Water Supply' (Macmillan), *c.f.*, L. i./14,398.

**EXCESS LIME METHOD** of treating water is effective for sterilising and purifying, and when necessary softening, water.

Liming the Dee as a means of overcoming sewage pollution.—

The Aberdeen water is soft (2° Clark's scale) hence the amount of Lime necessary is relatively smaller than would be required with the London water. Three parts per 100,000 were used. The method is very efficient in killing off *B. Coli*. Before the liming *B. Coli* was found in 1, 5, 10, 50, and 100 Cc., and on four occasions (during 8 days) not at all, whilst after the liming there was a run of 18 days in which no *B. Coli* was found in 100 Cc., and when the lime was stopped *B. Coli* appeared again.—B.M.J. ii./13,140.

**Miguel's Standard.**—Pure water may contain 100 to 1,000 or



ganisms per Cc., very impure being defined as containing 100,000 and upwards.

Sewage (Crude).—Total organisms in London sewage found to be 6 to 12 millions per Cc. *B. Celi* never fewer than 100,000 per Cc. —Klein and Houston.

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## CHEMICAL AND BACTERIOLOGICAL EXAMINATIONS OF DRINKING WATERS COMPARED.

It appeared of great importance to determine the relationship existing between chemical and bacteriological reports on Drinking Waters. It is common knowledge that a water may pass certain standards chemically and yet be unsatisfactory from the bacteriological aspect. The converse may also be true in some cases.

We instituted recently a research on these lines and in the following table we bring together the more important data which we have obtained chemically and bacteriologically.

The Waters dealt with comprise a representative selection of Drinking Waters as supplied *from the main* to private consumers in some of the leading cities and health resorts in Great Britain. The selection includes, for example, the supplies of London, Glasgow, Bath, Blackpool, Buxton, etc., etc.

For certain reasons we omit the names of the cities in several cases.

TABLE OF COMPARISON OF CHEMICAL AND BACTERIOLOGICAL EXAMINATIONS OF DRINKING WATERS CONDUCTED IN OUR LABORATORIES, SEPTEMBER TO NOVEMBER, 1913.

Source.	Chemical.				Bacteriological.										Our Conclusions.		
	Ammonia. Parts per million.		Free.	Alb.	Chlorine parts per 100,000.	Solids parts per 100,000. and effect on ignition.	Bacteria per Cc.		Volume pro- ducing Acid and Gas in MacConkey Broth with		Rosindol Reaction.	Indol Reaction.	Fluorescence on Reibel- agar plates.	Acid and Clot in Litmus Milk.		Motility.	
							Gelatin at 20° C.	* Agar at 37° C.	Glu- cose†	Lac- tose‡				Acid Clot.			
Water No. 1	1.	Nil.	0.02	0.06	3.	4.	5.	6.	7. Cc. 10	8. Cc. 10	9.	10.	11.	12.	13.	14.	15.
					1	Much charred on ignition	100	160			+	+	+	+	+	+	Chem., Good. Bact., Not satis- factory.
No. 2 Bath			0.02	0.034	2	36 slight charring	972	8	100	100 50 acid only.	—	—	—	+	+	+	Chem., Excellent. Bact., Satisfactory.
No. 3			Nil.	0.06	1.5	12 slight charring	1,209	57	10	50	—	+	+	+	+	+	Chem., Good. Bact., Satisfactory.
No. 4 Buxton			0.03	0.12	1	15 much charring	45	80	No acid or gas w h 100 Cc	No acid or gas with 100 Cc	—	—	—	—	—	—	Chem., Safe organi- cally. Bact., Excellent.



No. 5 .....	0.026	0.056	5	45 very slight charring	172	199	10	10	+	+	+	+	+	+	+	Chem., Good. Bact., <i>Not</i> satis- factory.
No. 6 .....	Nil.	0.026	3	30 not charred	1,109	37	50	50	—	+	+	—	—	—	—	Chem., Excellent. Bact., Satisfactory.
No. 7 .....	0.026	0.03	1	3 charred	at least 1,000 some liquefing	820	10	10	—	—	—	—	+	+	+	Chem., Excellent. Bact., Might be better.
No. 8 .....	0.08	0.12	1.5	18 charred	at least 1,000 some liquefing	1,600	50	50	—	—	—	—	—	—	—	Chem., Safe organi- cally. Might be better.
No. 9 .....	0.01	0.036	6.5	45 very slight charring	1,040	242	50	50	—	—	—	—	—	—	—	Chem., Excellent. Bact., Satisfactory.
No. 10 Village Well A Ditto B.....	0.08	0.168	10.5	70 charred	10	60	1	10	+	+	+	+	+	+	+	Chem., Unsatis- factory. Bact., Bad.
	0.026	0.12	10.5	68 charred	B. Sub- tilis pre- vented count	75	100	100	+	+	+	+	+	+	+	Chem., Unsatis- factory. Bact., Satisfactory.
No. 11.....	Nil.	0.11	1.5	6 Much charred	3,000	50	10	10	+	+	+	+	+	+	+	Chem., Safe organi- cally. Bact., Unsatis- factory.

Source.	Chemical.				Bacteriological.										Our Conclusions.	
	Ammonia. Parts per million.		Chlorine parts per 100,000.	Solids Parts per 100,000. and effect on ignition.	Bacteria per Cc.		Volume pro- ducing Acid and Gas in MacConkey Broth with		Rosindol Reaction.	Indol Reaction.	Fluorescence on Reibel- agar plates.	Acid and Clot in Litmus Milk.		Motility.		
					Gelatin at 20° C.	Agar at 37° C.	Glucose†	Lactose†				Acid Clot.				
	Free.	Alb.	1.	2.	3.	4.	5.	6.	7. Cc. 100	8. Cc. 100	9.	10.	11.	12.		13.
No. 12 London A	Nil.	0.04	1	32	less than 10	20	20	100	100	+	-	-	+	+	+	{ Chem., Excellent. Bact., Satisfactory.
London B	Nil.	0.03	1	32	Nil.	21	21	100	50	+	+	+	+	+	+	
No. 13.....	Nil.	0.08	2	21 slight charring	1,400	1,350	10	10	10	+	+	+	+	+	+	Chem., Good. Bact., Not satis- factory.
No. 14 Margate	Nil.	0.04	2.5	30 not charred	800	30	10	10	10	-	-	-	-	-	-	Chem., Excellent. Bact., Satisfactory.
No. 15 Norfolk (A Private well be- fore re- pair)	0.026	0.076	4	40	52	32,000	1/100	1/100	1/100	+	+	+	+	+	+	Chem., Org. safe. Bact., Bad.
Ditto (after repair)	0.1	0.07	4	36	70	157	10	50	50	-	-	-	+	-	-	Chem., Org. safe. Bact., Great im- provement, now safe, subject to supervision.



No. 16.....	Nil.	0·03	3·2	30 not charred	at least 1,000 liquefy- ing	820	10	10	—?	+	—	+	+	+	Chem., Excellent. Bact., Unsatis- factory.
No. 17.....	0·02	0·015	70	210 much charred	at least 1,000 liquefy- ing	410	100	100	+	+	+	+	+	+	Chem., Unsatis- factory. Bact., Unsatis- factory.

\* Pathogenic and intestinal organisms grow best at this temperature.

† Presumptive evidence of *B. Coli*, *B. Paratyphosus*, *B. Enteritidis*, but excluding *B. Typhosus* and Dysentery Organisms.

‡ Confirmatory for *B. Coli* as *B. Typhosus*, *B. Paratyphosus*, *B. Enteritidis* and Dysentery organisms do not give it.

Columns 7 to 13 include the "Flaginac" Reaction.

Columns 9, 10 and 14 show results of tests made on cultures in peptone water from the least quantity of MacConkey's Broth Culture showing acid and gas.

**Official Reports in comparison with our findings.**

Medical Officers of Health in certain instances kindly provided us with their recent Analytical reports and we append some details.

**Water No. 1.**—This water supply is at the time undergoing complete reorganisation. *B. Coli* had been found in 50, and in 10 Cc. and sometimes in 1 Cc. during stormy weather.

**Water No. 9.**—A report stated chemically and bacteriologically of the highest quality. Organisms 10 to 14 per Cc. No *B. Coli*. in 1 Cc.

**Water No. 11.**—A report stated : 1 to 3 organisms per Cc. on incubation at 37° C. *B. Coli* absent from 1 Cc. Water very good bacteriologically.

**Water No. 13.**—A report stated : No evidence of contamination. —June 24th, 1914.

**Water No. 14.**—A report stated : Free Ammonia nil, Albuminoid Ammonia "0·0006" (presumably per 100,000), Chlorine 2·65 —December, 1913. Bacteriologically 5 to 7 organisms per Cc. capable of growth at 22° C. and no organisms capable of growth at 37° C. in 2 Cc. *B. Coli* absent from 60 Cc.—Examined July, 1914.

**Water No. 16.**—A report stated "fulfills chemically and bacteriologically every requirement that would be regarded as desirable in a model supply."

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We are of opinion that marked divergence would be found, especially in the bacteriological findings between examinations at the source of supply—lake, reservoir, etc. and from the main taps in private dwellings. This factor explains in great measure the differences between our reports and the "Official" data provided by Public Health Authorities.

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**Conclusions.**

The conclusions we may draw from our own investigations are :—

(1). The bacteriological investigation is more useful than the chemical—and should at any rate always accompany a chemical examination.

(2). The absence of *B. Coli* from 100 Cc. of a water is an ideal seldom attained.

(3). The albuminoid ammonia content is no indication of the number of bacteria.

(4). Examination of waters at the source and after traversing some miles of water supply pipes may shew marked differences.

Speaking generally, we were gratified to find these Town supplies of good quality.

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**Swimming Bath Water.**—It was found that the water in question on entering the bath contained 43 organisms per Cc. Coli-form or intestinal organisms were present in 5 Cc. but not in 1 Cc. Water from the 1st class bath after 194 people had been in it gave 2,850 organisms per Cc. Coli-form organisms present in 5 Cc. The 2nd class bath after 767 persons had been in it gave about 15,000 organisms per Cc. Coli-form or intestinal organisms in 0·5 Cc. water, but not in 0·1 Cc. On another occasion twenty times the quantity of organisms were found in the 2nd class bath. Further examinations showed that the average number of organisms in two samples of 1st



class was 110,000 per Cc., and the average in three samples of 2nd class was 126,000 per Cc. Though many more individuals had used the 2nd class bath the water was not so very much worse than the 1st class,—the organisms in both cases were both pathogenic and non-pathogenic. Recommendation to empty the baths more often.—L. ii./10,542,578.

## MILK ANALYSIS.

### Average Chemical Composition:—

Water approx.=87.44%. Milk fat approx.=3.81%; Non-fatty solids, 8.75; including the following, Lactose (average 4%); Protein (Casein average 3.5%); Mineral matter. Milk also contains small quantities of Citric Acid and Enzymes. (See Enzyme Table.)

The following data are necessary to determine quality of a specimen.

- (1) **The Specific Gravity** may be determined by a Specific Gravity bottle or Lactometer; the average reading is 1.031.

N.B.—Low gravity may indicate added water, or in some instances richness in fat.

- (2) **To Determine Total Solids.** Evaporate 5 Gm. of the specimen on a water bath in a tared platinum capsule; the residue, which should be nearly white, averages 12.8%. Minimum: 11.5%.

- (3) **Fat.** Two determinations at least should be conducted, particularly if the figure for the non-fatty Solids is to be taken as the difference between the Fat result and that of the Total Solids. The following method is convenient:—

Shake the milk and place 10 Cc. of same in a Schmidt tube (graduated to 50 Cc.) and provided with a cork. Add 10 Cc. Hydrochloric Acid. Heat corked 10 minutes on water-bath shaking occasionally; then cool rapidly under water stream, when quite cold fill the tube to 50 Cc. mark with ether (pure). Insert cork and shake vigorously 1 minute, allow to separate and read off the volume of ether. Remove 2 separate 10 Cc. and evaporate in tared dishes. Take the mean and calculate % of fat. *It must not be less than 3%,—vide infra.*

(With regard to this 3% Milk Fat Standard it is known that the yield from the same cow may vary greatly, *e.g.*, it may be 2½% in the morning and as high as 4½% in the afternoon. The milking should be done at equal 12 hours intervals as far as possible.)

Cream in normal milk is about 10% varying with season, pasture, etc.

Milk that has been adulterated with water throws up its cream readily. Refrigeration of Milk prevents cream rising. Milk that has been Pasteurized will not throw up its cream at all.

### Non-fatty Solids

Are determined by subtracting the fat content from the Total Solids. *Mus not be less than 8.5%.*

### Lactose, or Milk Sugar Estimation (Average content 4%).

Dilute 50 Cc. of sample with water 150 Cc., add a few drops of Acetic Acid to throw out Casein and Albumin, boil for a short time and after cooling make up to 250 Cc., finally allow to stand and filter. 5 Cc. of the filtrate represent 1 Cc. of the original milk. Into 5 test tubes marked '1' to '5' place 5 Cc. of freshly mixed Fehling Solution: dilute with an equal volume of water and add from a burette to '1' 3 Cc., to No. '2' 3.5 Cc., to No. '3' 4 Cc., to No. '4' 4.5 Cc., to No. '5' 5 Cc. of the above filtrate, place on a sand bath and boil for six minutes. According to the colour of the supernatant fluid in the tubes one notes whether the reduction is complete. It may be necessary to repeat the test, using intermediate quantities, *e.g.*, 4.1, 4.3, &c., Cc. of the filtrate. The calculation is on the following lines:—

In an experiment 4.15 Cc. of the filtrate were necessary. 1 Cc. of Fehling Solution = 0.00675 Gm. Lactose ∴ 4.15 Cc. Filtrate = 0.03375 Gm. Lactose, *i.e.*  

$$\frac{4.15}{5} \text{ Cc. Milk} = 0.03375 \text{ Gm. Lactose} \therefore 100 \text{ Cc. Milk} = \frac{0.03375 \times 5 \times 100}{4.15} = 4.07 \text{ Gm.}$$

Lactose.

### Lactose Determination by Polarimeter:—

Add to 60 Cc. of the Milk 10 Cc. of a solution of Mercury in twice its weight of Nitric Acid 1.43 diluted with four times its volume of water. Make volume

up to 102.4 Cc., filter. Note rotation in 200 m.m. tube,—divide by 2 and by 53 the specific rotation for lactose. Result is the amount of lactose per Cc. in the solution. Multiply by 100 to give the amount in 60 Cc.—P.J. ii./04, 850.

**Mineral Matter** of milk can be obtained by igniting the milk solids, and usually averages 8.3% of them.

*N.B.*—A dilution of normal milk with water will reduce the ash almost proportionately to quantity of water added, so the combination of a low ash and low non-fatty solids point strongly to addition of water.

**Casein Estimation** (Average content 3.5%).—Dilute 20 Cc. of the sample with 300 Cc. water, and add strong acetic acid drop by drop to complete precipitation. Pass in carbon dioxide for 20 minutes, collect the casein and fat on a weighed filter paper; wash thoroughly with, firstly, alcohol, then ether to remove fat (well conducted in a Soxhlet thimble on water bath), dry and weigh.

For method of estimating proteins by Kjeldahl's process, see P.J. ii./04, 851.

Many proteins are precipitated by Acetone, Weyl applied this property to estimation of the Proteins in cow's milk and in fresh bullock's blood and obtained concordant results. The milk or blood is diluted with equal volume of water and poured into four volumes of Acetone. The precipitate is collected, washed with equal volumes of Acetone and Water then with Alcohol and is finally extracted with Ether in a Soxhlet apparatus, dried and weighed—J.C.S.A. i/10, 287.

**Lecithin** contained in various milks. Human, average, 0.0499%, cows' 0.0629%, asses' 0.0165%.—P.J. ii./08, 840 See also p. 76.

**COLOSTRUM.**—The milk from mammals shortly after birth of their young differs from normal milk in containing a very high percentage of an albumin closely resembling blood albumin. The proteins it contains are soluble. Colostrum provides readily absorbable nutriment, as the infant's stomach contains no gastric juice at the commencement. It is highly laxative in properties, probably owing to its high fat content.

The fat content of the fæces of the infant is always high—ranging from 10 to 20%—during the first week it is as high as 40 to 50%.

The salts in human and cow's milk vary very greatly. Nearly  $\frac{1}{3}$  of the salts of cow's milk are alkali citrates and alkali earth citrates. Human milk contains 0.5 Gm. of Citric Acid as citrates, whilst cow's milk contains from 1 to 1.5 Gm. per litre.

The proteins of Milk consist almost entirely of Casein and Albumin. Analyses show mean percentages as follows:—

	Casein. ('Lactalbumin.')		Maximum.	Minimum.
Cow's Milk ..	6	1	7 to 1	4.5 to 1
Goat's ..	3	1	3 to 1	2 to 1
Sheep's ..	3	1	4 to 1	3 to 1
Mare's ..	1.5	1		
Asses' ..	1	2.3		
Human ..	1	1		

The proportion of these two forms of Protein is adjusted to the needs of the animal, the albumin being easily digested, and the casein digested with difficulty. A sixteen pound infant requires more casein than one weighing 12lbs, though of the same age, and the human milk changes accordingly. More and more casein and less and less albumin is required by the child as time goes on.—Am. Jl. Ph. Feb./08, 55. c.f. Whey Powder, Vol. I., p. 543.

The milk supplied in this country in a large proportion of cases is from cows in calf. That from cows not in calf is more digestible, as the drain of the embryonic calf interferes with quality of the pregnant cow's milk.—L. ii./08, 1554.

**Milk, Cream and Butter Preservatives.**—The most commonly occurring are:—Salt, Sodium Bicarbonate, Boric Acid, Formalin, Hydrogen Peroxide, and Glycerin.

The Board of Agriculture in 1901 issued certain 'Sale of Milk Regulations' which require a minimum of 3% milk fat, also at least 8.5% milk solids other than fat. Skimmed or separated milk to have at least 9% milk solids.

Taking advantage of the exceedingly low standards laid down by the Board of Agriculture it appears that farmers are making an additional profit by



toning down milk with skimmed or separated milk so as to keep the fat content just within the standard. Suggestion that this should be overcome by revision of the Regulations.—B.M.J. ii./10,1178.

**Milk and Dairies' Bill** introduced into the House of Commons by Mr. J. Burns. Provisions for more effective registration and inspection of premises used by milk traders, prohibition of milk likely to cause infectious disease (including tuberculosis). Registration to be made compulsory.—L. ii./12,1735,1762.

The Bill ordered by House of Commons to be printed Dec. 10th, 1912. Prof. Delépine's Criticisms.—L. i./13,343.

A Milk Bill added to the Tuberculosis Order is essential if we are to make any real headway in warfare against surgical tuberculosis. Stamp out bovine tuberculosis.—H. J. Stiles, B.M.J. ii./13,371.

Milk Supply Control by clean milking, etc. Necessity of adopting Bang's method,—i.e., to isolate in a farmer's herd those cows afflicted with tuberculosis and to feed the calves of those born of diseased mothers with the milk of those not affected and to continue so as to raise a non-tuberculous herd.

For a number of references to previous Bill,—the 'Pure Milk Bill,' see Edition XV., Vol. II., p. 186.

Farmers should be forced by legislation to more sanitary measures. Highly unsatisfactory condition of London's supply.—W. Colingridge, M.O.H. City of London, L. /ii.13,822.

New Milk and Dairies Bill introduced into the House of Commons by Mr. H. Samuel (Pres. L. G. B.), May 12, 1914.—*Vide* L.i./14,1474.

For the legal requirements as to Butter, Cream, etc., "The Law and Chemistry of Foods and Drugs," Robinson and Cribb (Rebman) may be consulted.

**The Sale of Food and Drugs Act, 1875-1899**, enforces that any food may be sold providing no false description be given, that the article is in accordance with purchaser's demand, and that no substance be incorporated so as to render the article injurious to health.

The following are amongst the offences: Section 3 of the 1875 Act: To mix, colour, stain, or powder any article of food with any ingredient or material so as to render the article *injurious to health*, Section 6, to sell any food or drug not of the nature, substance and quality demanded. (No offence is committed if the added matter is not injurious to health, but is required for its production or preparation as an article of commerce, in a state fit for carriage or consumption, etc.).

'Sale of Food and Drugs Act,' 1899 (62 & 63 Vict. ch. 51):—

Section 1 virtually enacts that if there is imported into the United Kingdom any of the following articles, Margarine, Margarine-cheese, Butter-milk, Cream, Condensed, Separated or Skimmed Milk, or any article of food adulterated or impoverished the importer shall be liable, unless the same articles be imported in packages or receptacles conspicuously marked with a name or description indicating that the article has been so treated.

Further Sections deal with the method of marking packages. An article of food shall be deemed to be adulterated or impoverished if it has been mixed with any other substance, or if any part of it has been abstracted so as, in either case, to affect injuriously its quality, substance or nature, but an article of food shall not be deemed to be adulterated by reason only of the addition of any preservative or coloring matter of such nature and in such quantity as not to render the article injurious to health.

The Departmental Committee's Blue Book issued in 1901 and Dr. Hamill's recent report on Preservatives in Cream should be consulted.

Hamill states (C.D. ii./09,473) that "Thickeners" such as *gelatin*, *starch-paste* and *sucrate of lime* have been used for cream. Mixtures of *Boric Acid* and *Borax* mixed in such proportion so as to be neutral, have been used as preservatives. *Saccharin* is used to mask incipient sourness. *Sodium Salicylate* and *Benzoate* are also used in the hope of their being overlooked after the *Boric Acid* (which is allowed to the extent of 0.25%) has been detected. *Formalin* is unsuitable, *Sodium Fluoride* is used and is thought dangerous, *Hydrogen Peroxide* is also employed—100 Cc. of 3% to each gallon maintained at 120° F. in a closed vessel for 1½ hours, then 1 or 2 drops of 'Catalase' added to decompose excess of

Peroxide. Dealers in 'Jug Cream' think the Boric Acid permitted is insufficient.

According to recent work in U.S.A. Sodium Benzoate should be the least harmful of all.

**Milk Preservatives.** Public Health (Milk and Cream) Regulations 1912. The Local Government Board drafted regulations under the Public Health Acts coming into force June 1st, 1912, which will apply to the whole of England and Wales, *prohibiting the use of preservatives in milk*. They provide that "no person shall add, or order or permit any other person to add, any preservative substance to milk intended for sale for human consumption, and that no person shall sell or expose or offer for sale, or have in his possession for the purpose of sale, any milk to which any preservative substance has been added."

### **Cream Preservatives.**

Regulations defining conditions under which preservatives may be used in cream containing (previously) 40% or over of fat were withdrawn.—L. i./12,592,1558.

**New Regulations** which came into force October 1st, 1912, provide that the addition of Boric Acid, Borax or a mixture of these, or of Hydrogen Peroxide is *not prohibited in cream containing 35% or over of milk fat* (no preservative may be added to milk or cream containing less than 35% fat), but a system of declaration is required to be followed by all dealers after January 1st, 1913.—L. ii./12,399, i.e., (i.) This cream must be sold as **Preserved Cream**, not as "cream." (ii.) The vessel in which it is sold must bear a declaration of the amount and nature of the preservative used.—L. ii./13,1268.

There is no limit placed on the quantity of any of the three preservatives permitted, but the percentage of Boric Acid must be declared on the label. This, it is thought, will encourage producers to limit the use to the smallest quantity possible.—L. ii./12,961. (? W.H.M.).

Any person selling preserved milk or cream contrary to these regulations will be liable to conviction under the Sale of Foods and Drugs Acts.—P.J. i./12,283.

Experiments show that Boric Acid 1 in 2,000 and Formaldehyde 1 in 50,000 preserve milk for 24 hours. Refrigeration and pasteurisation preserve without intervention of these chemical aids.—B.M.J. i./05,1412.

Filtration by means of sand has been suggested. This is largely done on the Continent.—B.M.J. i./08,936.

**Ortho - Methyl Amino - Phenol - Sulphate**, or **\*Ortol** (which is a mixture of this body with Quinol and is used in photography) are recommended for milk testing. One Cc. 1% solution is added to 10 Cc. of milk and followed by 1 drop of ordinary '10 volume' Hydrogen Peroxide. Raw milk, or milk that has not been heated above 75° C., gives a reddish pink colour.—B.M.J. i./03,664.

Tests for Ortol.—P.J. i./07,429.

### **Budde Process of Preserving Milk.**

Consists in adding 15 Cc. of a 3% Solution of Hydrogen Peroxide



to 1 litre of Milk and warming to 51—52° C. for at least three hours. 48° C. is not sufficient and 55° is too high.—L. ii./05,209.

'**Mystin**' a preservative used for milk, cream, etc., on analysis was shewn to consist of Sodium Nitrite 9·85%, Formaldehyde 0·30% in Water. Dr. Monier Williams calculates that a quart of milk treated with the preservative in the proportion directed would contain 2 grains of Sodium Nitrite (*i.e.*, the maximum pharmacopœial dose). The presence of the Nitrite "masks" the detection of presence of Formaldehyde in the milk. After heating the acidified milk with a little Urea the presence of Formaldehyde can then be easily detected or distillation with Phosphoric Acid will set free the Formaldehyde.

'**Accoine**' was found to contain Sodium Benzoate 13·97% and Sodium Carbonate 1·94%. A preservative for Margarine was found to consist of Sodium Fluoride. In detecting the presence of Fluorides the value of the Titanium Test is pointed out, which depends upon the bleaching action of Fluoride Compounds upon a Peroxidised Titanium Solution.—the orange-yellow color of which is partially discharged in presence of Fluorine Compounds.—B.M.J. i./12,384,512, L.i./12,446. P.J.i./12,395.

It is held that *preservatives may prevent milk from tasting sour*, whilst at the same time *not inhibiting the growth of many kinds of disease germs*. According to the new order of things, 'sweet' milk purchased in the hot weather will be in reality fresh, and being fresh the chances that it is contaminated with disease bacteria will be greatly reduced.

### Detection of Boric Acid in Milk (*will preserve, 1 in 500*).

This, the most frequently employed preservative is detected by evaporating and incinerating at least 10 Gm. of the milk. Acidify the ash slightly with dilute hydrochloric acid (using Litmus). A strip of turmeric paper is now placed in the capsule, so as to be only partly wetted by the liquid. Evaporate to dryness at 100° C.

If boron compounds are present, the part immersed in the liquid will turn brownish-red (formation of rosocyanin). On moistening with a drop of caustic soda, green and purple colours will be produced. On re-acidifying with hydrochloric acid, the red colour is restored, and is again changed to green and blue with excess of alkali.

The flame test is well-known. Evaporate to dryness, treat the ash with a few drops of strong sulphuric acid, add a little methyl alcohol, and apply a light. The alcohol will burn with green at the edges of the flame (at the moment of ignition more particularly). We have determined Boric Acid 1 in 5,000 with ease by this method using 10 Cc. of the sample. It will show even 1 in 8,000 but with some uncertainty.

Borax and Boric Acid cannot be differentiated as Borax alone without the use of Sulphuric Acid gave the colour even though the ash of the milk alone was alkaline to Phenolphthalein. If Boron is found titration of the Ash would be the only means of concluding in which form it existed by comparing with an average milk residue Boron free.

Toxic Symptoms.—Gas in the stomach and intestines, colic, pain in the epigastrium and diarrhœa may be caused by excessive consumption of Boric Acid.

Possible cause of increase of appendicitis.—Campbell Williams.

### Detection of Formalin in Milk.

A teaspoonful will preserve 10 gallons of Milk for 3 days in hot weather.—Pharm. Form.

A large addition can be detected by simply warming; but it is better to distil the milk; the distillate has the odour of formaldehyde, but the preservative is not wholly volatilised even when evaporated to dryness at 100° C. In employing colour tests for formaldehyde a notably weaker reaction is obtained when milk containing formalin is distilled and the distillate tested than when water containing the same proportion of formalin is similarly treated.

O. Hehner has determined the rate of disappearance of formalin when added to milk. He found that after one week no formalin could be detected in a sample which originally contained 1 part of formalin in 100,000 parts of milk; after two weeks none could be found in the 1 : 50,000 sample; while after three weeks there was only the faintest trace to be detected in the 1 : 25,000 sample. The experiments were made in cool weather, and the formaldehyde was tested for by Schiff's reagent in the distillate from the milk.

The best and simplest test is the **Phloroglucin Test** (*infra*), but Schiff's and Hehner's Test are used.

**Schiff's Reagent.**—Mix 40 Cc. of a 0.5% solution of magenta with 250 Cc. of water, add 10 Cc. of sodium bisulphite solution Sp. Gr. 1.375, and then 10 Cc. of pure strong sulphuric acid; allow to stand for some time, when it will become colourless. It may also be prepared when required for use by adding sufficient of a solution of sulphurous acid to decolorise some of the magenta solution. If the sulphurous acid is added in large excess, traces of formaldehyde will not be indicated. Reddish violet colour proves presence of formalin. *Other aldehydes, including aromatic aldehydes, also give the reaction; but these would hardly be suspected.*

*It is better to distil as above mentioned or to use Hehner's Test, i.e., purplish violet ring on layering milk on to strong sulphuric acid; but this is also a group reagent for various aldehyde bodies.*—*Am. Jl. Ph. Aug./09, 394.*

The presence of Formalin 1 part in 200,000 can be detected with this Test also by the following modification:—

If to the distillate from a sample of milk one drop of a dilute aqueous solution of Phenolis added and the mixture poured upon some strong Sulphuric Acid in a test tube, a bright crimson ring appears.

**Phloroglucin Test.**—To 5 or 10 Cc. of the milk add 5 drops of 1% aqueous phloroglucin solution; shake and add 5 drops Liquor Sodæ 30%. Salmon colour (not yellowish tint) indicates addition of formalin. *We found recently that this test will show 1 of Formaldehyde (actual) in 50,000 of milk.*

**Rimini's Test.**—A satisfactory confirmatory test, being almost specific for Formaldehyde. For method of applying see 'Formaldehyde in urine' p. 236. *We found recently this test will show 1 of Formaldehyde (actual) in 100,000 of milk.*

Formaldehyde added to foods tends to derange metabolism. Wiley in United States investigated the effects of doses of 100-200 milligrams of Formaldehyde (given with milk) on 12 men during 15 days, the total being 2.5 Gm. to each man. Burning in throat, itching rash, retardation of Nitrogen and Sulphur metabolism, acceleration of phosphorus metabolism, and loss in bodyweight were observed. Apart from harmfulness as a milk preservative, its use is inadvisable, as in dilute solution it prevents the growth of acid forming bacteria, while not retarding many harmful organisms.—*L. i./09, 411.*

## BACTERIOLOGICAL EXAMINATION OF MILK FOR SUSPECTED SEWAGE OR FÆCAL CONTAMINATION.

Proceed on the lines of a water examination and draw conclusions from the isolation of *B. Coli*. It must be remembered, however, that even the finest and purest milk may show chance contamination of this description. A milk collected with the most stringent precautions in dealing with cows, stables, etc., might possibly show no *B. Coli* at all per Cc. The presence of a considerable number of *B. Coli*, for example 100 per Cc. with the simultaneous presence of *Streptococci* would be grave cause for suspicion of fæcal contamination, e.g., in the stables. Again, the presence of *B. Coli* may indicate a diseased udder, for example, mastitis, on the other hand the presence of *B. Coli* would in all probability not be caused by the animals drinking *B. Coli*—infected water.

The organisms found in milk may be classed as follows:—(i.) Acid producing (100 varieties), the principal member of which is *B. acidi lactici*; (ii.) *B. acidi butyrici* (has very resistant spores, not killed by pasteurisation); (iii.) those responsible for fermentation to alcohol, as koumiss, butter milk, red milk, blue milk, &c.; (iv.) the mould *Oidium albicans* produces thrush in infants' mouths; (v.) *B. tuberculosis* (a large percentage of cows are tuberculous); (vi.) *Streptococci* associated with contagious mammitis; (vii.) *B. diphtheriae*; (viii.) *B. coli communis* and *B. typhosus*.—*B. & C.D. ii./05, 576.*

See also **B. Tuberculosis in Milk**, p. 347.

Normal milk contains polynuclear and polymorphonuclear leucocytes, which may be mistaken for pus cells, as many as 54,300,000 per Cc. have been observed in an apparently normal sample. It is concluded that mere cell counts do not afford a true criterion of pathological condition of the udder; on the other hand a paucity of cells might also indicate a pathological process.—*M.P.C. i./14, 457.*



Various forms of apparatus are in the market for detecting adulteration of milk, *e.g.*, The **Lactometer Cream Tube** and **Lactoscope**—the last mentioned detects by the optical properties of milk its adulteration with water—or removal of cream.

**CONDENSED MILK** should have a minimum of 32% of total milk solids with 10% of fatty solids.

"**THE NATIONAL LEAGUE FOR PHYSICAL EDUCATION AND IMPROVEMENT**" issues leaflets to instil into the minds of all concerned in production and consumption of Milk simple rules required to ensure purity and cleanliness of milk.—L. i./11,123.

"Turning" of milk during thunderstorms accounted for by the usually prevalent high temperature and moisture content of the air favourable to bacterial growth rather than by electrical disturbance.—P.J. ii./12,345.

## BUTTER ANALYSIS.

**Average Chemical Composition of Unadulterated Butters :**

Water 6.5 to 11.2, Curd 2.4 to 3.1, Salt 1.6 to 2.0, Fat 83.7 to 89.5%.

The following data are necessary to determine quality of a specimen.

- (i.) **Estimation of Water**:—Heat 5 Gm. in an air-oven to 110° C. The loss should not exceed 17%, if more suspect careless making or intentional adulteration.
- (ii.) **Estimation of Curd and Salt**:—Melt the residue of (i.) and treat with 10 Cc. ether, filter through tared filter, repeat the process and wash until all ether-soluble matter is removed, dry residue and weigh; the residue consists of curd and salt.
- (iii.) **Estimation of Ash**:—Ignite residue from (ii.) and weigh. Should be wholly salt; confirm this by standard Silver Nitrate solution.
- (iv.) **Estimation of Fat**:—Should be taken by difference by subtracting the sum of percentages of water, curd and salt from 100.
- (v.) **Detection of Foreign Fats**:—Prepare some butter-fat by melting 8 Gm., pour off and filter through dry filter, being careful not to pour any of the water on to same. Saponify on a water-bath 5 Gm. of the clarified fat in a tared flask, capacity about 250 Cc. marked at 150 Cc.; add 50 Cc. Alcoholic Solution of Potash (3%) and distil off the alcohol. Dissolve the residual soap in a little hot water, add 25 Cc. Sulphuric Acid (5%) and make up with distilled water to 150 Cc., add a little pumice and capillary glass tubes and distil off 100 Cc. filter same and titrate with  $N/10$  NaOH (using Phenolphthalein). 5 Gm. pure butter-fat should require not less than 25 Cc. of alkali; lard, tallow, beef-fat, &c., require only about 1.5 Cc., coconut fat would require about 7 Cc.

### Exception.

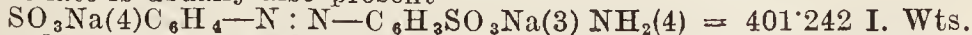
In the winter some butters require only about 21 Cc. of alkali, the sample should therefore not be condemned unless it requires less than the minimum amount.

In 15 samples of **Margarine** vegetable oils to the extent of 40 to 90% of the total fat were found—in most cases it was Coconut Oil. The food value of all animal and vegetable fat is the same—both yield 9.1 Calories of energy per Gm.—B.M.J. ii./11,959,1336.

## Anillin Dyes used in Colouring Foods.

**Egg Yellow.**—*Syn.* Acid Yellow.

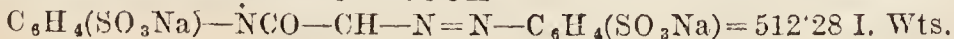
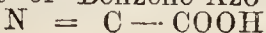
The Sodium Salt of Amido-Azo-Benzene-di-Sulphonic Acid. Some Mono Sulphonate is usually also present



A reddish-yellow powder *soluble* in water—aqueous solution has a neutral action, mineral acids change the colour to a bright red, yellow being restored by the addition of alkali. Used for colouring milk (1 in 200,000), Egg Powders—Custard prepared for table contains about 1 in 40,000.

**Lemon Yellow.**—*Syn.* Tartrazine.

The Sodium Salt of Benzene-Azo-Pyrazolone-Carboxy-Disulphonic Acid



A yellow powder, *soluble* in water, almost unaffected in colour by Acids or Alkalies. When Tartrazine is reduced Sulphanilic Acid is formed. Used for colouring lemonade and similar beverages, a common proportion being 1 in 500,000.

#### Annatto Substitute.

Is a mixture of Acid Brown No. 1 (10 parts) and Acid Yellow (8 parts). *Acid Brown* is the Sodium Salt of Para-Sulpho-Benzene-Azo-Metatoluylene-Diamine (4) ( $\text{SO}_3\text{Na})\text{C}_6\text{H}_4\text{N}:\text{NC}_6\text{H}_2(\text{CH}_3)(\text{NH}_2)_2(1.5.2.4)$ .

A dark brown powder with occasional yellow specks dissolving easily in water. The solution has a neutral reaction and is of a dark red colour, becoming yellow when greatly diluted. Mineral Acids change the solution to a bright red. Alkalies return original colour.

Used for the same purposes as the vegetable colour (has approximately 25 times the tinctorial power of the commercial extracts of the fruit, of which 1 tablespoonful is added to 30 lbs. cheese, *i.e.*, 1 part in 960) for tinting Milk, Butter, Cheese (1 in 24,000), Haddocks, etc.

**Bixæ Folia, Ph. Ned. (*Bixacacæ*).** The leaves of *B. Orellana*. Annatto is obtained from the seeds.—N.S.D. p. 242.

**Annatto Extract.**—Bixin related to *m*-xylene is the essential colouring matter. The Extract is usually strongly alkaline.

General conclusions of the investigation appear to indicate that in the amount used Egg Yellow, Lemon Yellow, and Annatto Substitute are harmless.—S. Rideal, L. i/II, 1597, 1656.

### CARBON MONOXIDE AND DIOXIDE TESTS.

Frequent deaths have recently occurred from Carbon Monoxide poisoning. Ordinary Coal Gas and Carbon Dioxide are also sources of danger.

WATER GAS and PRODUCER GAS are used for motive power of engines and for heating purposes, whereas for general lighting CARBURETTED GAS alone or Carburetted Water Gas mixed with Coal Gas is used.

PRODUCER GAS is made by passing air or a mixture of air and Steam through Incandescent Coke or Anthracite Coal in a furnace generator, as in the Dowson producer. Consists of Hydrogen, Nitrogen, Marsh Gas, and CO with  $\text{CO}_2$  as its principal impurity.

WATER GAS is made similarly, except that steam only is passed through the Coke, and the product being chiefly Carbon Monoxide and Hydrogen,  $\text{C} + \text{H}_2\text{O} = \text{CO} + \text{H}_2$ .

CARBURETTED GAS differs from both the above. It is made by passing water Gas made as above over heated refractory material charged with oils rich in hydrocarbons. The volatilised benzene and benzene congeners mix with the Water Gas.

Coal Gas contains .. .. .	6-9% CO.
Producer or Water Gas .. .. .	25-50% ..
Carburetted Gas .. .. .	30% ..

—L. ii./o6, 1578, 1649 (including treatment).

The following test will indicate one part of Carbon Monoxide in 10,000 parts of the atmosphere. Even  $\frac{1}{4}$  to  $\frac{1}{2}$ % of the gas is most injurious, and if inhaled for some time may be fatal (Schmidt).

10 to 20 litres of air are aspirated for about 15 or 20 minutes through 10 Cc. blood (fresh) diluted, 1 to 10 with water. The blood is then heated to the boiling point in a flask, and a current of air is passed into it which has previously passed through a solution of Palladium Chloride.\* The air, which passes out of the blood, is then led into bottles containing Lead Acetate Solution, diluted Sulphuric Acid, and another quantity of diluted Palladium Chloride Solution, in this order.

The presence of Carbon Monoxide in the air under examination is proved by the deposition of reduced Palladium metal in the last mentioned Palladium Chloride solution. A quantitative method on this principle is based on the fact that 106 parts of Palladium deposited are equal to 28 parts of Carbon Monoxide.

Note.—The blood used for the absorption of the Carbon Monoxide, is to be heated immediately after the aspiration with the air under examination and the passing of the air is to be continued three or four hours.

\* Palladium Chloride in 3% aqueous solution. *Dose.*—5 to 10 minims before meals. Has been advocated for use in treatment of tuberculosis of the lungs. Said to improve appetite, and diminish the fever and coughing. Contra-indicated in nervous and neurasthenic patients.



The gas may also be detected by the aid of the spectroscope

Deaths from effects of Carbon Monoxide.—L. i./03,258; L. i./04,394 L. ii./05,1894; L. ii./10,879,1693.

Estimation of Carbon Monoxide.—P.J. ii./11,787.

### Detection of Carbon Monoxide in the Blood.

In addition to the spectroscopic method, Kimkel's Colour Test is valuable.

Necessary are a pipette, 2 small test tubes, and a 3% Tannin Solution.—For details of method see Dix and Mann's Forensic Medicine.—B.M.J. i./05,1382.

Increase of Carbonic Oxide in illuminating gas.—L. i./04,1427.

Carbon Dioxide.—Haldane's apparatus is used for estimation in the air

Nickel Carbonyl, causing degeneration of certain parts of the nervous system, produced three deaths.—L. i./03,269,1842. Latest examination of the compound and effects of. Iron Carbonyl is less toxic.—L. ii./07,907. Symptomatic treatment and purgation cured a case of nickel poisoning in a metal worker caused by nickel dust being absorbed.—L. i./08,40.

The poisonous symptoms are occasioned by the absorption of the nickel set free. Nickel Carbonyl poisoning is a particular case of nickel poisoning. The nickel is deposited over the immense surface of the lungs in a condition especially favourable for its absorption.—L. i./09,487. Probably as a hydrated sub-carbonate.—B.M.J. i./09,52.

### Antidote.—Oxygen.

For treatment of persons who have inhaled these noxious gases, fresh air, sulphur baths, good food with quinine and Nux Vomica, Chloroform Liniment with friction for local neuralgia and commencing neuritis.—L. i./03,337; ii./03,117.

Chlorine inhalation and taken internally employed. Early and judicious use of this (by action of Hydrochloric Acid on Potassium Chlorate) should be successful. Oxygen was unavailable in this instance (a case of coal gas poisoning from a gas bracket).—L. i./07,1155.

Interesting Experiments at the London Hospital (June, 1910), on 6 students showed that Carbon Dioxide (4%) is not poisonous but injurious effects due to stagnant condition of the air and moisture.—*Fanning* the air caused resuscitation.

Carbon Monoxide poisoning in the Senghenydd explosion.—B.M.J. ii./14,57.

## PTOMAINES.

Under this name are classed a number of basic substances which are produced in meat, fish, and albuminoid food undergoing putrefaction by decomposition or by bacterial metabolism. They are akin to the alkaloids, several being dangerous poisons. Hence the occasional outbreaks of ptomaine poisoning from the consumption of meat pies, fish and the like.

*Symptoms* are those of gastro-intestinal irritants, but they may resemble those of Atropine poisoning. Dryness of the tongue, thirst, dilated pupils, debility, with probably rigors, offensive diarrhoea, high temperature, sickness with convulsions.

*Tyrotaxon* occurs in stale cream, cheese, milk products; causes vomiting, purging, rapid pulse, dyspnoea, depressed temperature and prostration.

*Antidotes*.—Give emetics and Castor Oil, then stimulants. Amyl Nitrite, Strychnine, Digitalis, Caffeine, Sal Volatile, Tannic Acid, and Atropine hypodermically.

For Fish Poisoning give Potassium Chlorate or Liquor Ammoniae Acetatis, also Tinctura Capsici and Spiritus Chloroformi.

Presumed Ptomaine poisoning from tinned fish.—L. ii./03,755,848.

Poisoning by bad bacon treated with Calomel, and later injections of Atropine and Strychnine.—B.M.J. i./06,258.

Outbreak of illness due to tinned meat in Carlisle. The meat (American Corned Beef) reported as bacteriologically unfit for food. It was proved to be contaminated previous to, or at the time of, canning in America.—L. ii./10,1613.

## II.—EXAMINATION OF STOMACH CONTENTS.

An extended series of examinations proves that in a healthy subject food commences to pass the pylorus in from fifteen minutes to half an hour after ingestion, the time varying with the character of the food (e.g., carbohydrates

leave the stomach before proteins), and the stomach is empty in five hours. *The passage through the small intestine takes about three and a half to five hours, about one inch a minute, so that there is food in the cæcum before the whole meal has left the stomach.*—H. W. Carson, Oct., Pr., 1912.

An **Outfit** is arranged containing the necessary **Reagents** and **Apparatus**. The **Reagents** include Blue Litmus Paper, Congo Red (an anilin colour turned blue by acids and red by alkali, the reverse of Litmus, indicates absence of Hydrochloric Acid in the stomach in cases of cancer, as weak Lactic Acid does not interfere), Benzopurpurin Paper, Alizarin Solution, Dimethyl-amido-azobenzol Paper and Solution (an acid and alkali indicator which is not affected by Carbon Dioxide—a 1 in 500 Alcoholic Solution of the compound is used in ordinary chemical testing), Decinormal Soda Solution, Ether, Caustic Potash Solution, Phenolphthalein\* Solution (1 in Alcohol 90%, 300 with Distilled Water to 500, is reddened by alkali, but is not suitable for ammonia estimation), Cupric Sulphate Solution, Lugol's Solution, Methyl Green and Methyl Violet and other Test Solutions.

**Thymophthalein.**—Dissolves in caustic alkalis forming a blue colour. May, therefore, be used as an indicator—is not affected by excess. To prepare heat Thymol 3, Zinc Chloride 2.5 and Pthalic Anhydride 3, for 6 hours at 115 to 120° C. Break up when cold and remove Thymol with Steam. Dissolve in Caustic Soda and pour solution into dilute Hydrochloric Acid, wash precipitate with water and crystallise from Alcohol.—P.J. ii./13,881.

The **Stomach Tube** should have bevel-edged eyes, known as "velvet eye." Van Valsh's tube has the smaller eye of the two which should be on a level with and opposite the upper border of the other; this arrangement prevents possible blocking of the tube and injuring the lining of the stomach.

**Aseptic Lubricant Glycerin Jelly**, is used for assisting the passage of these tubes. A Glyco-gelatin Pastil of Menthol, gr.  $\frac{1}{12}$ , with Cocaine Hydrochloride  $\frac{1}{16}$  grain, is also useful to be sucked just before passing.

**Inflation of the stomach for diagnostic purposes** is best carried out by the double bellows of a spray apparatus attached to a stomach tube.

A method of inflation is by giving first Tartaric Acid, 30 to 90 grains in water, followed immediately by 40 to 120 grains of Sodium Bicarbonate, and another is by Auto-inflation by means of Spivate's tube.

**Portions of stomach contents are removed** to examine for acidity, to ascertain the presence of food, mucus or gastric secretion, when it should normally be empty; to examine test meals and to search for pus, blood and bacteria.

**Dunham's Tassel** consists of a little tassel of thread soaked in Dimethyl-amido-azobenzol Solution. It is attached to a thread, the patient swallows it, it is removed after an interval, and the resulting colour gives the condition of the stomach as regards free Hydrochloric Acid.

**Turck's Capsule** consists of a hard Gelatin Capsule, No. 00, enclosing a small rubber tube attached to a thread for withdrawing, and provided with strips of Congo Red, Blue Litmus and Dimethyl-amido-azobenzol papers; after swallowing and withdrawing, the resulting colours will be:—

1. If stomach contents neutral no change in colour of any of the Papers.
2. If no free acid, but only combined acid and acid salts, the Litmus will be red and the others unaltered.
3. If there be free organic acid but no free Hydrochloric Acid, the Congo Red will be blackish blue, but the Dimethyl-amido-azobenzol Paper will be unchanged.
4. If free Hydrochloric Acid present, all the Papers will be changed—the Litmus red, the Congo Red blue, and the Dimethyl-amido-azobenzol Paper will be red.
5. If both Hydrochloric and Lactic Acid be present, the Congo Red Paper will have a blackish tinge.

\***Phenolphthalein** is employed as an indicator in volumetric analysis as it turns pink with alkalis. It is not suitable for titration of ammonia. It is the best indicator for inorganic and organic acids, remove CO<sub>2</sub> by boiling. Where CO<sub>2</sub> is evolved Methyl Orange (q.v.) is better, but this is not satisfactory with organic acids.



The rubber tube will contain sufficient material for microscopic examination, *e.g.*, for the Oppler Boas Bacillus or Sarcinæ.

By means of a **Silver Stomach Bucket** a small quantity, *i.e.*, about 2 Cc. may be lifted up out of the stomach and examined. By **Turck's Aspirator Bottle**, which is exhausted by means of a bulb, the stomach contents flow into the bottle. This is one of the simplest methods of removing stomach contents.

The **Water Test** for myasthenia consists in introducing into the stomach 300 Cc. of water first thing in the morning, fasting, and 1½ hours afterwards another 100 Cc. containing 1% of glucose. In due course a small quantity of the stomach contents are removed and the sugar estimated (p. 236, *et seq.*), from which is determined the amount of the original 300 Cc. remaining in the stomach.

**Ewald's Test Breakfast** consists of two or three ounces of dry bread and 10 ounces of hot water, or weak tea without milk or sugar. The Lactic Acid in bread vitiates the results where the presence of this acid is of importance, as in the early stages of cancer.

**Boas's Test Breakfast** (given after lavage) consists of one full tablespoonful of oatmeal to a quart of water, reduced to a pint by boiling. There are a variety of other tests (meat and bread) meals.

The following are abstracts from the works of Willcox, Herschell, Martin and others :—

**Chemical Examination of the gastric contents after a test meal**, containing little proteid and nitrogenous bases.—Willcox, L. ii./o8,220 :—

The Hydrochloric Acid in this case will be present as far as possible in the free condition (which is the point of importance in diagnosis of gastric ulcer).

**I. Total Acidity** (Normally=0.15% HCl). Determine whether there is active Hydrochloric Acid or a mixture of this and organic acid. Usually in chronic gastritis acidity is low. In *gastric ulcer it is high*. In *carcinoma it is usually low*. (A normal acidity does not exclude gastric carcinoma.)

It is increased in simple hyperchlorhydria, peptic ulcer, cholelithiasis, appendicitis, and colitis.—L. i./13,462.

Increase in the mineral Chlorides may be an earlier sign of carcinoma than the diminution of the active acid. The condition may be accounted for by the secretion of an alkaline fluid in the stomach—probably by a malignant growth that has begun to ulcerate.—Q. Jl. Med., Apl., 1911,334.

Without doubt both total acidity and free Hydrochloric Acid are raised in a considerable proportion of ulcer cases. Duodenal cases show on an average a larger and more constant increase of acidity than the ulcers on the gastric side. Discussion on gastric ulcer.—B.M.J. ii./12,940 *et seq.*

**Litmus Paper** is affected by Hydrochloric, Lactic and Butyric Acids.

**Congo Red Paper**. As already stated—the colour caused by organic acids will disappear on warming over spirit lamp whilst that due to Hydrochloric acid remains.

**II. Hydrochloric Acid**, This, according to Willcox, is either (a) free, (b) combined with protein and organic bases (*i.e.* physiologically active), or (c) **Inorganically** combined (*i.e.*, physiologically inactive). Normally free HCl is 0.1%.—B.M.J. ii./12,940.

(a) **Phloroglucin test for free Hydrochloric Acid (Günzburg)** :—

Phloroglucin 2 Gm., Vanillin 1 Gm., Alcohol 90% 30 Gm. A rose red colour formed on warming a few drops with an equal amount of the specimen in a porcelain dish indicates presence of the Acid. May also be best kept in powder form—2 parts of Phloroglucin and 1 part of Vanillin. As much as will lie on the point of a penknife, added to a few drops of alcohol, forms a perfectly reliable solution. This is the most trustworthy.

This test is positive with free mineral acids and may be relied on to show the absence of Free Hydrochloric Acid.—L. ii./12,1104.

Response to **Dimethylamidoazobenzol** may be given by organic acids if these are present in large amount. The latter may be used first, followed by Günzburg's test as confirmatory. If the test meal has been such as to give the Hydrochloric Acid the opportunity of being present in the free condition, then in normal gastric contents it will usually be present.

In *gastric ulcer* and hyperchlorhydria always present ; in *carcinoma* scarcely ever present.

**Boas' Test for Free Hydrochloric Acid.**—Resorcin 5, Cane Sugar 3, Alcohol 100. This test is used exactly as Gunzburg's test, the same red color being produced, but Boas' requires heating more carefully, as it chars more readily and the color is not permanent.

(b) **Physiologically Active Hydrochloric Acid.** *i.e.* Free and combined with protein and organic bases (normally about 0.15%).

**Willcox's Modified Volhard Method.**

Two equal quantities of gastric contents are taken, one rendered alkaline with soda,—both are evaporated and ignited. In one case the *Total Hydrochloric Acid*, and in the other the *Hydrochloric Acid combined with inorganic bases* only is obtained. Difference gives *Active HCl*. In gastric ulcer and hyperchlorhydria the *Active HCl* is equal to or nearly equal to the total acidity, and is usually over 0.15%. In gastric carcinoma the *Active HCl*, as found by Willcox, is nearly always much reduced,—always under 0.1%. In chronic gastritis the *Active HCl* is often below normal.

**Differential Estimation of Physiologically Combined and the Free Acid.**

The fluid is titrated with Alkali in presence of Dimethyl-amidoazobenzol as indicator, the result being the physiologically combined + Free Hydrochloric Acid; then another portion is titrated with Alizarin Red (1% Aqueous Solution) as indicator, which gives Free Hydrochloric Acid only. The amount of alkali required in first titration minus the amount required for the second titration is the amount required by the *Physiologically Combined Hydrochloric Acid* *i.e.* Hydrochloric Acid combined with proteins and other weak bases, *e.g.*

1st titration showed 0.2% calculated as Hydrochloric Acid.

2nd titration showed 0.15% Free Hydrochloric Acid.

$0.2 - 0.15 = 0.05\%$  Physiologically Combined Hydrochloric Acid.

Gastric Contents, Acidity Estimation.—H. L. Tidy, L. ii./12, 1104. Reply upholding the accuracy of Volhard's method by G. Graham and R. L. Mackenzie Wallis *ibid* 1460.

**III. Organic Acid, Lactic Acid.** According to Willcox great importance should not be attached to presence or absence of this acid. Organic Acids in considerable amount are present in carcinoma of the stomach and where much fermentation is going on. By others, again, the presence of Lactic Acid is considered of grave importance, especially if in considerable quantity, *v. infra*.

Lactic Acid is not present in the normal stomach. If found is suggestive of carcinoma.—H. W. Carson, Pr., Oct., 1912.

**Uffelmann's Test for Lactic Acid.**—(not entirely satisfactory). Ferric Chloride Solution 1 drop, Phenol 0.4 Gm., water to 50 Cc. (Delicacy limit 1 : 10,000—the violet colour changes to yellow.)

An approximate estimation may be conducted as follows:—

Distil off 30 Cc. from 40 Cc. of the filtered stomach contents the total acidity of which is known. The volatile acids go over; the residue contains the Lactic and Hydrochloric Acids. The acidity of the distillate (found by titration with  $N/10$  Soda, using Phenolphthalein as indicator) deducted from the total acidity "A" (found by titrating 10 Cc. of the filtered stomach contents in the same manner, the result being expressed in terms of Hydrochloric Acid) gives the amount of Lactic and Hydrochloric Acids together. If the amount of HCl "H" (found in the same way as "A," but using Dimethyl-amido-azobenzol as indicator) be deducted from this, the remainder is **Lactic Acid**.

**IV. Mucin.** Important. In gastric ulcer and hyperchlorhydria usually absent. In gastric carcinoma a definite precipitate occurs on adding 2% Acetic Acid. In simple gastritis often present in small amount.—Willcox. It is soluble in Sodium Hydrate Solution. Dried film is deeply stained reddish violet by Thionin Staining Solution.

**Mucus** normally is stained faintly, but that met with in chronic gastritis deeply with Methyl Green.

**Blood** is recognised microscopically.

**Ferment Activity.** Determination of Pepsin and pepsinogen present is of great importance. Willcox has devised a **NEW METHOD**:—

Action on milk by determination of the activity of the gastric juice by **Rennin** contained (usually proportionate to Pepsin) by using a series of tubes containing 5 Cc. of milk, to which are added gradually increased quantities of the gastric juice, and the mixtures maintained at 40° C. for 30 minutes. About 0.2 Cc. of normal gastric juice (of the adult) is required in this test.

In *gastric carcinoma* much more.



In *gastric ulcer* and hyperchlorhydria usually less (0.05 or less).

In certain cases it may be necessary to estimate **Renninogen**,—consult the paper.

**Rennin** is tested for by adding a few drops of the filtered and neutralised stomach contents to two or three Cc. of milk and maintaining the mixture at 98° F. for a quarter of an hour, resulting coagulation indicates presence.

For testing for **Rennin Zymogen**, a small quantity of Calcium Chloride is added prior to incubation. A pocket incubator may be used for these experiments.

Tables in which the analytical data had been obtained are provided of cases of :—

(1) gastric ulcer and hyperchlorhydria, (2) gastric carcinoma, (3) mucous colitis (4) stomach normal, (5) chronic gastritis, (6) gastric ulcer.—L. ii./08,220.

Digestive activity of the stomach contents (*i.e.*, amount of Pepsin secreted) increases or diminishes with the amount of Hydrochloric Acid secreted by the mucous membrane. A number of cases of gastric carcinoma compared with cases of ulcer and functional disease showed that on the whole the greater proportion of cases evidenced a great diminution of acid secreted, as well as diminution of digestive power.—S. Martin, L. i./09,398.

#### Simple methods of Diagnosis in Disease of the Stomach :—

This paper differs in some particulars from the views of the previous writer.

For practical purposes, as all that is required to know is *whether the free Hydrochloric Acid is normal, subnormal, or excessive*, the author has devised a special tube for estimating. To the point "A" on it a filtrate of gastric contents is introduced. A drop of mixed Phenolphthalein and Dimethylamidoazobenzol is added, then drop by drop N/10 NaOH Solution till the red colour has disappeared. The marks on the tube show whether the amount corresponds to a normal, sub-normal or excessive value for *free HCl*. N/10 NaOH is again added till the red colour of the *Phenolphthalein* appears—this gives the *Total Acidity*.

When there is free Hydrochloric Acid it is no use testing for Lactic Acid.

When there is normal total acidity lactic acid is rarely present, but when no free Hydrochloric Acid and total acidity is low *Lactic Acid* must be tested for. Lactic acid denotes subacidity combined with stasis due either to pyloric obstruction or fermentation due to an ulcerating growth. These two factors occur together in carcinoma and rarely in other diseases. A well-marked reaction with **Uffelmann's Test** (*q.v.*) must be obtained to be any evidence.—L. i./09, 526.

In gastric ulcer, results with test meals indicated in the majority of cases excess of free Hydrochloric Acid.—L. i./09,764.

Contrary to Prof. Moore, Copeman and Hake find the physiologically active Hydrochloric Acid in mice and rats with transplanted or spontaneous tumors, is not only not diminished, but for the most part is in slight excess above the normal.—L. i./09,755.

Cancer in stomach and liver found by exploratory operation after free Hydrochloric Acid has disappeared from the gastric contents.—B.M.J. i./09,650.

Free Hydrochloric Acid is diminished in many cases of carcinoma of the stomach. In 10% of cases it is increased. L. i./09,915.

Considerable diminution helpful in diagnosis of ? gastric carcinoma.—B.M.J. i./09,829.

The estimations of little value in early cases.—B.M.J. i./09,833.

The diminution of the gastric Hydrochloric Acid is general in cancer, not only of the stomach, of any origin.—Hewlett, P.J. i./13,248.

The **Oleic Acid Method** of diagnosing gastric malignant disease, *r.p.* 289.

**HYPERCHLORHYDRIA AND ITS COMPLICATIONS.**—W. Russell was the first to clearly differentiate hyperchlorhydria from other gastric ailments. The purpose to which Hydrochloric Acid is applied is in acting with Pepsinogen. It is said that digestion never fails from deficiency in Pepsinogen because of its great power even in small quantity. The symptoms of hyperchlorhydria are burning pain at the cardiac orifice of the stomach, acid eructations, water-brash, usually flatulence and constipation. In some cases there is a sense of dragging or weariness or a hunger discomfort coming on two hours or less after breakfast, and removed by taking a glass of milk, a drink of cold water or soda-water or a cup of tea. Somewhat later in life there is much gastric discomfort or definite pain coming on an hour or two after a meal. This is associated with mental depression and great difficulty, amounting in some cases to complete

incapacity, for mental or physical effort. On removing the gastric contents in such cases they are found to be intensely acid and to contain much free hydrochloric acid. That this hyperacid fluid is the cause of the pain and depression is proved by the immediate relief of the symptoms when it is withdrawn. A *simple test* in Scotland for digestive conditions is the following:—If *porridge and milk cause acidity* the digestion is not right. Sodium Bicarbonate not only counteracts the free Hydrochloric Acid, but also inhibits acid secretion. For inhibition of secretion Belladonna is best.—B.M.J. ii./10, 1914.

Some authorities are of opinion that *no such condition* as hyperchlorhydria really exists, and that an ordinary "acid dyspepsia" due to an excessive secretion of normal gastric juice is capable of causing most of the symptoms ascribed somewhat indiscriminately to hyperchlorhydria and duodenal ulcer. This opinion is strengthened by the fact that estimates of free Hydrochloric Acid have proved inconsistent.—B.M.J. ii./11, 1918.

The pain of GASTRIC ULCER has been attributed to an excess of Hydrochloric Acid acting on the affected membrane. 0.5% Hydrochloric Acid applied to an abrasion of the skin produces smarting and might be expected to cause pain in a gastric ulcer, but was quite tolerated when 4 ounces were introduced into the empty stomach by a tube where gastric ulcer was subsequently diagnosed by operation. Similarly HEARTBURN has often been ascribed to the regurgitation of the Hydrochloric Acid into the œsophagus, but some observations negated this also; nevertheless the Acid is in some way evidently connected with the production of the pain, as Alkali relieves it.—L. i./11, 1915.

### Nitrogen Factor.

The Phenolphthalein and Dimethylamidoazo-benzene readings of acidity are employed to give what is termed the Nitrogen Factor. In an active stomach "*Phenol*" minus "*Dimethyl*" reading is a constant under Normal Test Nitrogen meals, etc. A certain multiple of this constant—the Nitrogen Factor is normally about 2.4. A rise above this indicates stasis or impairment of the digestive process. Table of 19 cases presenting appendicular disturbance.—C. Singer, L. ii./12, 1911.

Test for the products of **Starch Digestion**. The presence of Erythro-dextrin in any quantity (giving a brown colour with Lugol's Solution) one hour after a test breakfast will point to hypochlorhydria.

**Gunzberg's Capsule**, for testing digestive power, consists of  $\frac{5}{16}$  inch of thin rubber tubing,  $\frac{1}{8}$  inch in diameter, containing  $1\frac{1}{2}$  gr. Potassium Iodide plugged with pledgets of Fibrin at each end.

**Fermentation** is examined by means of an ordinary Doremus Ureometer.

Estimation of the **digestive power** of the gastric juice is effected with hard boiled egg by examining for peptone after two hours or so at 40°C.

### Peptic Index.

**Edestin**, a substance made from Linseed, is purified by recrystallisation from warm salt solution. It is soluble 1 in 60 of 0.2% Hydrochloric Acid, 1 in 25 of 0.5% Sodium Hydrate, about 1 in 460 of 4% Sodium Chloride. Much more soluble in the last mentioned at 65° C.—which constitutes its method of manufacture. The purified preparation is dissolved in the proportion of 0.1 per cent. in 0.12 per cent. HCl. Of this solution 2.5 Ccm. are poured into each of ten test tubes, and allowed to stand at the ordinary temperature of the room; 1 Ccm. of filtered stomach contents is diluted to 10 Ccm. and then 0.1, 0.2, 0.3, and so on, in a gradually increasing series up to 1, of diluted stomach contents are added to the solution in the tubes, which are shaken and allowed to stand for half an hour; at the end of this time 0.3 Ccm. of a saturated solution of common salt are added to each tube and the tubes again shaken; at a certain degree of concentration the solution remains clear, but with less digestion a white precipitate forms.

The following conclusions have been arrived at: (1) That the estimation of the peptic index by the Edestin method affords a useful help in the diagnosis of organic diseases of the stomach and duodenum. (2) That peptic index and the chloride secretion vary ordinarily in the same direction when the wall of the stomach is the seat of organic disease, and where there is an exception to this rule it generally occurs, we note, in the form of a relative lowering of the peptic index. (3) In the early stages of duodenal ulcer the peptic index is *ordinarily high* (over 60) and the secreted chloride also high (over 6); in the experience of the authors this is almost pathognomonic of duodenal or pyloric ulcer. (4) In the advanced and developed cases of duo-



denal ulcer the peptic index may be low; in very chronic cases the chloride secretion may also fall. (5) Cases of pyloric ulcer follow the same rule as cases of duodenal ulcer, but in the former the peptic index is ordinarily somewhat lower. (6) Gastric ulcers not seated at the pylorus show no definite alteration of the index, but it is ordinarily somewhat low. (7) Cancer of the pylorus generally leads to slight lowering of the peptic index and the chloride secretion, but in the early stages the chloride secretion may even be raised. (8) Cancer of the stomach which has spread to the small curvature from the pylorus causes always marked lowering of the peptic index and nearly always that of the chloride secretion. (9) Chronic appendicitis with gastric symptoms may be accompanied by organic changes in the stomach, but these may also be absent. A definite relative raising of the peptic index over the chloride secretion is met with chiefly in those organic diseases which are combined with appendicitis.—B.M.J. ii./13,885.

**Keratin Coated Hard Gelatin Capsules** (largest size) filled with **Bismuth Carbonate**, and **Chain Cachets** (2 inches of fine silver chain in a cachet attached to a piece of silk), are used for **X Ray examination** of the stomach. Barium Sulphate and Bismuth are also used, *c.f.* Vol. I., p. 202, 207, 211.

**Microscopic Examination** reveals starch, sarcinæ and the **Oppler Boas Bacillus**, present in malignant disease—stained with Methylene Blue. (It is Gram + staining.)

On **gastroscoy**—a plea for its routine employment by gastric experts. Topical applications by means of the method can be made to ulcers, portions of a tumour can be removed for microscopic examination and a pin or needle sticking into the gastric mucosa could be released or retrieved.—William Hill B.M.J. ii./09,843; B.M.J. ii./11,1074; see also Vol. I.

**Tropæoline OO** and **Methyl Orange** (Helianthin), *e.g.*, as Solution—Methyl Orange 0.4, Alcohol (90%) 50, Water to 200, are yellow colours used for testing for the presence of free acids. The former is changed to crimson by acids, the latter to pink, but no change is produced by Carbon Dioxide, Acid Carbonates or Metallic Salts. They are not suitable for Organic Acids

**Rosolic Acid**, *Syn.* AURIN, CORALLIN.

1% in 60% Alcohol. Turns Rose red with alkalis and yellow with acid. Remove CO<sub>2</sub>. It is not suitable in presence of NH<sub>3</sub>.

### III.—BACTERIOLOGICAL AND CLINICAL NOTES

#### with reference to Special Diseases.

[A cabinet is arranged containing the Apparatus, Stains and Solutions necessary for taking and examining Diphtheritic Scrapings, for detecting the **Gonococcus** in discharge, for staining Sputum for **B. tuberculosis**, for collecting Blood for **Widal's Typhoid Reaction**, for the Gram separation of Organisms, and for all other general clinical diagnoses.—B.M.J. ii./00,332; L. ii./00,1282.]

**Acne Vulgaris** (obtain specimen by puncture and decompression of papule or pustule).—A. Fleming (L. i./09,1035, B.M.J. ii./09,533) describes the bacteriology of acne vulgaris. Gram positive organisms which, when seen in pus, are arranged very irregularly. In 44% of the pus films examined only acne bacilli were found. Acne bacilli with *Staphylococcus* were present in 53%. The acne bacillus *Syn.* "**Bottle Bacillus**" stains less deeply than the cocci. The bacillus grows with difficulty on artificial media. A suitable medium for growing the organism was found to be Nutrient Agar containing 1 to 5% *Oleic Acid*. *Cultivation*.—Good results may be obtained by growing anaerobically in broth 3 weeks and then plating on Serum Agar with Neutral red and about 2% *Oleic Acid*. Vaccines have been prepared from a three weeks' culture on the above medium.

Sudmerson and Thompson use an acid Serum Agar taking the deeper parts of the comedo in which the bacillus usually predominates, emulsify this in Saline and spread thinly on the slope so as to obtain colonies to pick off.

*Cultivation from the comedo*:—

T. H. C. Benians recommends for making Vaccines to grow simply in a tube of broth—the comedo being removed to same and then covered with

Sterile Oil. *Staphylococcus Albus* will be present but is negligible—the bacilli out-growing these Cocci in about a week. The conditions are thought to resemble those in a sebaceous gland.—L. i./13,1801.

For details of *Acne Vaccine*, vide *Vol. I.*, p. 869.

### Actinomycosis.

A parasitic disease, due to the 'ray fungus,' first observed in cattle (wooden tongue), characterised by chronic inflammation, with or without suppuration, frequently resulting in formation of granulation tumours, especially about the jaws. Vide Potassium Iodide, *Vol. I.*, for treatment.

*To identify the fungus.* 1. Place specimen, pus or sputum, in a flat glass dish on a black surface. Remove the characteristic yellowish particles if found, and carefully tease out on a micro-slide or cover-glass. 2. Fix film over the flame, *s.a.* Stain by the Gram-Eosin method, *v.* p. 361.

The violet stained mycelium of the fungus as tangled webs or scattered filaments will be seen on a pink ground (leucocytes, epithelia, &c.), with a  $\frac{1}{8}$  inch or even  $\frac{2}{8}$  inch objective.

The "rays" (see M. and R., etc.) may be observed without staining, but the stained specimens are confirmatory and valuable for reference. N.B.—*They are not found in man—only the filaments.*

Primary ovarian actinomycosis, a case of. Only six cases on record. Here the ovary was the primary seat of infection, and hence unique.—L. i./09,758.

A case of actinomycosis (streptotrichosis) of the lung and liver successfully treated with vaccine. The vaccine in this instance was standardised by weight 1 Cc.  $\times$  1 mgr. "Antimycotin" (solid substance).—B.M.J. i./08,554.

A vaccine is suggested of strength 1 Cc. = 0.0001 Gm. Solid Substance as initial dose rising to 1 Cc. containing 0.001 Gm., repeated according to clinical symptoms.

Actinomycosis, the result of chewing a stalk of corn, treated by Vaccine. Initial dose  $7\frac{1}{2}$  millions, subsequently 5 millions—17 inoculations in all. Complete recovery.—J. Collie, B.M.J. i./13,991.

A case of Actinomycosis of the lungs.—B.M.J. i./12,302. Local lesions closely resemble tuberculosis.

**Ankylostomiasis.**—The worm producing this disease (*Ankylostoma duodenale*) is about  $\frac{1}{4}$  inch long and of a whitish colour. Its habitat is the small intestine of man, particularly that of the miner. It attaches itself to the mucous membrane, and no fewer than 1,000 of them have been obtained from one patient. The male and female worm are quite different in formation. The eggs produced by the female pass away from the patient—as many as 8,000,000 have been delivered by a sufferer in a single day—and the small thread worm escapes from the egg. Mines afford an excellent hatching place for the young larvæ. Hygiene and sanitary measures are alone necessary to stamp out the scourge.

Probably is not a blood sucker.—The ænemia it produces is probably due to toxins with a hæmolytic action.—L. i./06,1246,1623.

Blood counts in ankylostomiasis in Egypt—percentage of Eosinophiles small in comparison with European.—L. ii./08,303.

In Ceylon increase of the disease, introduced by Coolies from India. The "wet" zone of the island is more markedly affected than the "dry."—L. i./06,1271.

Discussion on ankylostomiasis. Anæmia caused is frequently profound, producing ultimate death. Milk diet for a day or two, then Calomel and saline aperient; following morning Thymol 20 to 30 grains in a cachet, repeated twice at 1 hour's interval, with another Saline 2 hours after the last dose.—B.M.J. ii./09,1350.

**ANKYLOSTOMIASIS—LIFE HISTORY** detailed, Mode of Infection, Duration of Infectivity. There are said to be two causative organisms. Most of the disease in the Southern regions of the U.S. and in Porto Rico was thought to be due to *Ankylostoma (Necator, Uncinaria) Americanum*, as distinct from the generally known *A. duodenale*. *A. Americanum* has not been identified in the Cornish mines. Where both species are abundant, individuals are often doubly infected. Methods of detecting eggs in fæces, *v.* L. i./11, p. 783. See also for Life history.—B.M.J. ii./09,779.

In goitre Thymol appears to act by destroying the living excitant or by reducing its numbers or activity in such a way that the production of toxic substances is lessened and the thyroid gland is relieved of the excessive demand



for its secretion which necessitated hypertrophy.—Maj. R. McCarrison, L. i./13, 369.

For further details on Thymol Treatment *vide* Vol. I., p. 770, Eucalyptus Oil, p. 362.

**Anthrax** (for Antitoxin, see Vol. I.).—*Bacillus Anthracis* was probably the first bacterium to be recognised, inasmuch as it was associated with splenic fever as long ago as 1849. It is responsible for 'malignant pustule' in man. If an animal die suspected of the disease the mode of examination is to cut off the ear and submit the blood from the same to bacteriological examination. The organism does not spore in the body of the animal, but if the air gain access, as in the case of an ordinary post-mortem investigation, the organism spores rapidly and hence becomes a grave source of danger.

Chemistry of the Toxin.—P.J. ii./05,331.

The organism almost invariably occurs as long filaments, particularly in broth cultures (is non-motile). It grows on all the ordinary media both at room and body temperature, and produces in gelatin 'stab' cultures, typical 'inverted fir trees' appearance. By growing at 42° C. a non-sporing form can be produced, which is the mode of attenuation for the immunisation of animals, as introduced by Pasteur. The spores retain their vitality and pathogenicity for years in the dry condition. Martin has shown that the organism produces an alkaloid which is the fever producer and an albumose which induces the coma. The malignant diseases which the organism produces in man have been satisfactorily treated by Sclavo's Serum (*q.v.*) or by excision. If not diagnosed in time the organism may invade the blood stream, causing death, with symptoms of splenic fever, but the spleen is not so enlarged nor the bacilli so numerous in the organs.

Changes which occur in growth of the organism.—B.M.J. ii./11,1665.

Staining of the blood may be conducted by Gram's method (counterstaining with Eosin), also by Alkaline Methylene Blue. It is Gram positive.

**Ultra Violet Rays** by prolonged action transformed Anthrax Bacilli into a new type of organism which produced a new disease when inoculated into guinea-pigs. Possibly, given rays of sufficient penetrative power anthrax may be transmuted in the living organism.—Mme. Victor Henri, P.J. i./14,527.

**Appendicitis**.—Common intestinal parasites seem to be associated with this disease, *e.g.*, *Ascaris lumbricoides* and *Trichocephalus dispar*. Chauvel has pointed out that appendicitis appears to be the most prevalent among meat-eaters, and notably beef-eaters. It is, on the other hand, unknown amongst Arabs or the Chinese. In religious communities in Brittany where meat is never eaten, appendicitis is unknown.

Disease of the vermiform appendix may be initiated more frequently than is commonly supposed by entozoa, *e.g.*, *Oxyuris Vermicularis* and *Trichocephalus Trichiurus* may prepare the way for bacterial infection.—B.M.J. i./10,42.

**Beri Beri.** *Syn.* A form of **Polyneuritis**.—This disease infests the Federated Malay States and parts of China.

**Etiology of**, if not its origin, has at least an intimate relationship with the consumption of white or "polished" rice. No case among 273 people on parboiled rice. No distinctive organisms found either in blood or urine. Ankylostomes were not found as associated with the disease.—L. i./09,451, 561. B.M.J. i./09,1007.

The addition of rice polishings to a diet of white rice is an effective preventive of the development of polyneuritis in fowls. Rice polishings comprise from 8 to 10% by weight of the original grain.—L. ii./10,1775.

**Leader on Beri-Beri**.—Are the symptoms the result of a nitrogen starvation or due to a toxin produced in the rice by some organism?—L. i./09,1333,1526.

'Overmilled' would perhaps be a better term than 'Polished' rice. Rice thus 'polished' is deprived of pericarp, subpericarpal layers and embryo or germ.—B.M.J. ii./11,1446.

It does not occur in races using partly milled "cured" rice. It has been found that the poorly nourished are more liable to contract it than those well fed.

**Treatment**.—Strychnine, Arsenic, and Silver Nitrate are in repute as soon as the muscular hyperæsthesia has subsided.—Sir P. Manson, 'Manual of Tropical Disease.' A routine which has found some favour is the following:—

Magnesium Sulphate 60 grains, Dilute Hydrochloric Acid 20 minims, Tincture

of Orange 1 drachm, Infusion of Calumba to 1 ounce. Thrice daily for a week, and repeat after a few days intermission.

If much œdema, the following may be of use :—

Solution of Ammonium Acetate 1 drachm, Potassium Nitrate 10 grains, Potassium Acetate 15 grains, Camphor Water to 1 ounce. Thrice daily.

If the heart shows signs of failure, a mixture of Digitalis, Ammonium Carbonate and Compound Spirit of Æther may be used with advantage.—Brooke, 141.

“Unpolished” rice contains 0·6–0·8% Phosphorus Pentoxide, the “polished” grains contain only 0·40–0·45%. Thus the polishing of rice in steam-mills removes substances essential for the nutrition of nervous tissue. Much could be done in prevention by improving the dietary—adding rice and wheat bran or substituting for part of the rice some other grain, *e.g.*, that of *Phaseolus Radiatus*—L. ii./II,535.

The Phosphorus content alone is altered, being on cured rice raised from some 2 grains to 4·5 grains  $P_2O_5$  per man per day.—B.M.J. i./II,1421.

The relation of the organic Phosphorus content of various diets to diseases of nutrition, particularly beri-beri. The salt meat met with in ships is said to have lost 50% of its Phosphorus under the pickling process—the deficiency of Organic Phosphorus in milled rice may be caused by the absence of some compound at present unknown.—L. ii./II,1087,1230.

The work carried out in the Institute for Medical Research, Kuala Lumpur has shown that deficiency of *Phosphorus* is not the cause of beri-beri,—experiments appear to prove that neither is a glucoside responsible.—L. ii./II,1364.

**Vitamine**  $CO(NH)_2C_{18}H_{18}O_6$  (?).

Is contained in rice polishings and in yeast. It has been shown to be the substance preventing polyneuritis. A few grains of pressed yeast are sufficient to cure a pigeon suffering from the disease. It is the sole curative agent (suggestions have been made that two substances co-operating together may be required.—*C.f.*, C. Funk, L. ii./13,83). It probably belongs to the Pyrimidine group and may be a constituent of Nucleic Acid.

Two methods of manufacture from Yeast are given.—B.M.J. ii./12,787.

Vitamines and malignancy.—Further experimental work on the growth of young animals by omission of certain constituents from their food.—B.M.J. ii./13,155.

Vitamines in general contain no Phosphorus, they are not fatty bodies and are distinct from lipoids. They are nitrogenous bodies (*e.g.*, the formula of one is  $C_{26}H_{20}O_9N_4$ ) and are regarded as the mother substances of ferments and hormones. They are destroyed in 10 to 20 minutes at a temperature of 120–130° C. and also by extreme dryness.—T. Johnson, P.J. i./14,573.

The neuritis-preventing principle is insoluble in Ether, it is not inorganic, it is not volatile, but is destroyed by heat. It is absorbed by charcoal and cannot be recovered by water, Absolute Alcohol or Ether. Five Cc. of an extract equal to 5 grains of rice polishings were sufficient to protect fowls subsisting on polished rice, but 2½ Cc. were not.—Review of Tropical Diseases.—Pr., Aug. '13,218. See also Casimir Funk, B.M.J. i./13,814, and H. Fraser and A. T. Stanton, L. ii./14,398.

### **Beri beri Prevention and Treatment.**

A safe and harmless rice, *i.e.*, one from which not more than the pericarp has been removed in the process of polishing will always yield 0·4%  $P_2O_5$ —this is a fair standard on the undried material. It is difficult to educate the labouring classes in India to the use of unpolished rice.

Cure of Beri Beri.—An adult accustomed to the use of polished rice would require 1.75 ounces of Polishings daily. The active substance is soluble in 91% Alcohol.

**Liquid Extract of Rice Polishings.** made with acidulated Alcohol of strength 1 Cc.=10 Gm. fat-free polishings. Another liquid Extract prepared more thoroughly was also tried (1=5). This contains less Alcohol in the finished product. Effectual in animal experiments (cocks). Dose for adult human beings 2 drachms.—A. T. Stanton, L. ii./12,1005; see also L. i./14,98.

**Antiberiberin** is a black fluid preparation of rice bran. *Dose.*—1 Cc. or more of 10% solution subcutaneously each day. It is also given in pill, capsule or powder form. *Dose.*—6 to 10 Gm. of powder, 3 to 5 capsules, and 30 to 45 pills daily. Rice Bran Powder 8 to 25 Gms., and Rice Bran Extract 1 to 2 Gms. are also given.—M., 1912.

Consult also *Nutrimenta* and *Phaseolus*.



## Blackwater Fever.

[Practical notes on treatment:—Calomel 5 to 10 grains, Effervescent Saline. Intravenous injection of Normal Saline Solution, Quinine in nutrient enema (not milk), also Digitalis, and Strychnine in the same form.—B.M.J. ii./07,1324.]

A case of malaria suffered from typical blackwater fever while under study in hospital. He had distinctly pyrexial periods all differing as to plasmodia, fever and hæmoglobinuria. There must be some subterranean factor at work—some process different from the usual processes of ordinary malaria.—Prof. Ronald Ross.—L. i./11,585.

Quinine, it has been stated, may bring on blackwater fever. This alone or malarial intoxication alone does not cause hæmoglobinuric fever—it is caused by one of these plus the toxin, accentuated during the course of one or more malarial attacks.—L. i./11,702.

Blackwater fever, Causation of.—Colonial Reports.—Some hold it is not directly related to malaria.—L. i./13,260.

*Treponema Spirillum Verticale* said to be the micro-organism of blackwater fever—this is greatly questioned.—B.M.J. i./12,340.

*Bacillus Botulinus*.—This organism is found in a certain kind of meat poisoning designated 'botulismus.' An obligate anaerobe, motile—produces gas which splits up the medium in glucose agar stab cultures. It is Gram+ staining. Has terminal spores.

Bacteria of Poisoned Meat.—B.M.J. i./05,1257.

## Cancer, Sarcoma, and other Malignant Tumours.

Imperial Cancer Research Fund.—9th Annual Report.—1910—1911.

An important point which is brought out is that "the increase of cancer during the last decade is referable to certain anatomical regions and not to others,—thus in males the increase is almost confined to the alimentary canal,—especially the stomach, while in females it mainly affects the same system, stomach and intestines, although the breast suffers also. Much has been done with regard to 'soil' investigation,—there would appear to be no special feature in it favouring the growth of cancer, for transplantable tumours grow as well in normal animals as in those in which they first appeared. Yet a spontaneous tumour can hardly ever be implanted into an animal in which there has arisen a spontaneous tumour. With regard to treatment, it has not been found possible to arrest growth of spontaneously arising tumours,—it is thought doubtful whether any real progress is to be made along these lines." Warnings as to irritation are repeated. Further, cancer is not "catching," and "cancer houses" cannot exist. Heredity plays a part in the development of cancer of the breast in mice. At all age periods the disease was more frequent when the mother, or either grandmother, or all three, had died from cancer of this organ. Resistance has not been induced either with an animal's own tumour or its own normal tissue. A number of cases of natural healing of spontaneous malignant new growths had been observed in mice affected with spontaneous cancer. "It is necessary to warn against needless alarm or the awakening of pessimistic anticipations of the outlook on future efforts to cope with cancer."—B.M.J. ii./11,171; L. ii./11,315,391. See also B.M.J. ii./11,1307; L. ii./11,1345.

The Fourth Scientific Report of the Fund showed that a portion of cancerous tissue transplanted to another part of the same body grows readily, while the attempt to graft it upon another individual is abortive or difficult. The cancerous overgrowth of tissue

is usually, and perhaps exclusively, in some part of the body which has been subject to continuous irritation. Cancer of the generative organs has not increased at the same rate as that for other organs, and most of the increases affect the higher age-periods predominantly.

E. F. Bashford points out that the increase of cancer is real and not illusory—it is not due to a spread of infection. The common virus cannot exist for cat, mouse, and rat sarcoma, nor yet for sarcoma and carcinoma,—out of a pure adeno-carcinoma a sarcoma may develop in a certain number of instances. Embryonic mouse skin has extraordinary power of affecting a complete protection against mouse mammary carcinoma.

Dresden International Hygiene Exhibition.—B.M.J. ii./11,766  
Cancer—Bradshaw Lecture on:—

The living cancer-cell is the essential part of every cancerous growth, for when the cell dies it is impossible for any of the parts, agencies, or faculties of cancer to be excited or developed. In a successful graft the centrally placed cells die, but the peripheral portion of the transplanted tissue excites the surrounding fibrous tissue to form a support (stroma) for the tumour, whose soft tissues are wholly developed directly from the implanted living cancer-cells of the graft. Transfer of cancer from mouse to mouse is impossible if the vitality of the cancer-cells is impaired by pounding or by heat. On the other hand, inoculated infective granulomata show the fundamental difference that it is the host-tissue itself from which further growth results. A study of the cancer-cells demonstrates that it is only a variation of a normal cell, for it possesses neither in structure nor in power anything not found in the healthy cell. The established facts show that cancer-cells possess a great power of continuous multiplication, retaining inherited limitations to type of cells among which they first appear, but they develop and differentiate but little and irregularly in a manner neither purposeful nor effective. Beckton has shown recently that the tissue-cells of man contain, with particular exceptions certain granules, known as Altmann's granules, which are invariably absent in the cancerous growth proper. If this observation is confirmed it will not only be a very useful diagnostic character, but will also establish a morphological difference between cancer-cells and most normal cells, and afford anatomical proof that the former are not embryonic cells.

The potassium content of the red corpuscles of cancerous patients is approximately double that of healthy persons, although the amount of sodium is unchanged. Bashford has effected the artificial conversion of the malignant tumour of carcinoma into the soft cellular growths of sarcoma. This, as also the intimate connection shown between cancer-cells and the cells of the individual, make one unable to recognise in cancer an independent growth, parasitic or otherwise.

Cancer is cell-life that is disorderly, irregular, and with a minimum of development. It is a result of a breach or failure of fundamental cell-law—a law so majestic that obedience to it results in perfect health and disobedience to it means all the inscrutable woes of the dread disease.

Cancer is undoubtedly a disease that generally arises in cells that are growing, or have grown old, thus in woman the breast and uterus are prone to cancer as they get old before the rest of the body. The different incidence of cancer in the two sexes is not a sex difference affecting all the body tissues, but is the result of the special liability to the disease of organs possessed by one sex only. A chart given in the paper clearly shows the close parallelism of the cancer curve, in women, and in their generative organs only (at 40 to 50 years of age), and the near approach of the curve for women, when we exclude disease of their generative organs, to that of men (at 50 to 60). Age, chronic irritation, x-rays, alcohol—all so-called causes of cancer—agree in being conditions that deteriorate the evolution of the individual cell and apparently lessen the latter's hold over the great primal cell-law. Cases of the disappearance of cancerous growths mentioned show that there is cure of cancer, apart from operative removal. "When the biologist shall know the laws that govern cell-growth, with a knowledge akin in its sweep and accuracy to that



of the astronomer, he will have the power to prevent, to control, and to cure cancer."—Sir Alfred Pearce Gould. B.M.J. ii./10,1836; L. ii./10,1665; C.D. i./10,933.

**Imperial Cancer Research Fund, 1912, Meeting and Report, including Fifth Scientific Report.** The questions of immunity and spontaneous recession of transplanted tumours dealt with.—B.M.J. ii./12,129.

**Imperial Cancer Research Fund, Eighth Annual Report (1909—1910).**

Statistics of 13,000 cases, examined microscopically, from hospitals in England and Scotland have been published. The methods suggested by various workers for serum diagnosis of cancer had yielded negative results. Attention had been paid to malignant growths in cattle. Histological types comprised the majority of forms met with in man. Frequency of primary carcinoma of the liver associated with cirrhosis and primary malignant growths of the suprarenal was of interest. Practically all mammary carcinoma of the mouse can be transplanted.

From observations showing the small proportion of successful transplantation of spontaneous tumours it is concluded that animals naturally the subject of cancer do not suffer from it because they present a soil uniformly favourable to the disease; on the contrary the circumstances associated with the appearance and growth of cancer are peculiar to the individual attacked. The cancer cell although highly dangerous to the individual in which it arises may hence be relatively innocuous to other individuals.—B.M.J. ii./10,205; L. ii./10,241, 265.

Mice immunised subcutaneously by injections of Tumour or of normal tissue are resistant to the implantation of cancer in internal organs. The immune state is one of general distribution throughout the organism and not of local occurrence at the site of the immunising inoculation.—L. ii./11,92.

In the **Third Scientific Report (Seventh Annual Report)** published October, 1908, injection of Trypsin was stated to have given entirely negative results.

No evidence proving hereditary transmission had been obtained (mice experiments). The law of age incidence in mice holds good in a manner comparable with that for mankind. No evidence to show that the disease in nature is conveyed by the transference of living cancer cells. (*c.f.*, Ninth Report). Fifty mammary carcinomata under propagation in the laboratory, all different. A much larger variety of malignant new growths exists than formerly supposed. Further detailed investigation as to manner in which animals may be rendered resistant to the inoculation of cancer. It was found that cells, whether cancerous or normal, which had been killed or disintegrated in any case, such as by chemical properties, or by heat, cold, crushing, &c., were entirely deprived of their power of conferring resistance—this in complete contrast to that obtained when the organisms of infectious disease were similarly killed or disintegrated, as in those the products retain poisonous properties and powers of inducing resistance. The action of Radium on normal and cancerous tissues without causing disintegration was of *special interest*. After applying Radium for an interval *within which no structural alteration could be observed in the tissues, they might be completely deprived of their powers of growing and immunising*. Abolition of vital properties with retention of histological structure and intactness of the cells. Experiments showed that the power to elicit these biological reactions was internally bound up with and dependent on the vital activities of the cells themselves. Until now the parallel behaviour of the normal and cancer tissue in these respects almost excluded the possibility of Radium having selective action on cancer tissues. Data from outlying parts of the Empire included in particular search for peculiar forms of *chronic irritation* associated with occurrence of malignant new growths in native races. A new and most interesting point from Egypt was the occurrence of cancer of the skin of the chest on the triangular area of the skin left bare by the clothing worn by the Fellahin.

No one would have conceived it possible that portions of the *mammalian organism could be kept growing* for a period four times the length of life of the whole animal. While some chance opportunity may yield results of immediate practical moment, the outlook in therapeutics in the meantime

is directed to preventing dissemination of metastasis.—E. F. Bashford General Superintendent's Report.—B.M.J. ii./09,151.

The chance of a man who reaches 35 eventually dying of cancer is 1 in 12, of a woman 1 in 8,—the figures for the two sexes are approximating as time advances.

A fragment of cancer tissue transplanted to a previously normal mouse induced an increase in the amount of physiologically active Hydrochloric Acid during digestion. Mice which had been apparently completely protected against the inoculation of cancer had developed the disease spontaneously.—B.M.J. ii./07,26.

Cancer occurs in nearly all vertebrata, not in the higher types only. The malignant growths in all are identical. Transmissibility from one lower animal to another of same species possible. Cancer is transmissible to others and has an external origin. Contamination by food. Cremation of all who die from cancer essential.—L. i./08,80.

Plimmer's bodies, which were considered peculiar to cancerous tissues, are also present in healthy reproductive tissues. This disposes of the idea hitherto held that Plimmer's bodies are parasitic organisms.—C.D. i/05,793.

Action of Mercuric Chloride, Iodide, Potassium Cyanide and Ammonium Fluoride on mice tumours. Chemical analysis of 300 tumours showed preponderance of Potash Salts and nucleo-proteid content associated with high virulence and rapid development.—B.M.J. ii./06,1548.

Living cancer tissues from English mice implanted on to newly imported foreign mice causes a certain amount of resistance to the growth,—only a small percentage of the inoculated mice develop tumours.—National Cancer Research Fund.

The final victory over cancer will not be solely by the knife.—B.M.J. ii./06,1681.

Tables giving relative frequency of cancer in various organs—male and female.—B.M.J. ii./11,1244.

Cancer, the role of fat in the etiology of.—It is possibly the tissue which plays an important part both in the etiology and certainly in the progress of the disease. Note the pigmented condition of the fat in some cases of carcinoma *p.m.* In operating on mammary cancer the oily and fluid state of the circummammary fat is very noticeable. In those cases where oophorectomy for inoperable mammary cancer produces disappearance of outward signs of the disease there is improvement in general health and increase in subcutaneous adipose tissue. **Chemical Examination of Fats**—normal human and cancerous, gave interesting data. The fats were extracted by heat and examined for Iodine Nos. with Wij's Solution—there was decided difference in human fat before and after puberty—44.477 average Iodine value (= % of non-saturated fatty acids) between 9 and 11 years, and 60.83 between 16 and 19. Fat in health gave average Iodine value 62.1 and in cancer patients 72.62. Protoplasm according to latest views is an emulsion of proteins and lipoids, *i.e.*, there are cell fats, and any causes that make them more fluid lead to degeneration and destruction. What effects an excess of non-saturated fatty acids in the cells of adipose tissue of a part may have on surrounding somatic cells must be a matter of conjecture. Further research and enquiry necessary.—L. i./11,1560.

**Immediate Microscopic Diagnosis of Tumours at the time of operation.**—Sir W. Watson Cheyne.—B.M.J. ii./08,972. *See also* L. ii./10,939.

*Diagnosis of Cancer by examination of the blood :—*

**Antitryptic Index.**—*The power of any given serum to inhibit tryptic digestion compared with that possessed by a normal standard serum.* The Antitryptic Index was found to be raised in 94% of cases of malignant disease. The reaction is, however, not specific, as most processes involving cell destruction produce a heightening of the index. The methods of obtaining the results are one chemical, another electrical, and a third by estimating viscosity of the serum.

Gastric ulcer can be distinguished from carcinoma of the stomach by the test. The electrical method registers more definitely than the chemical one,—details of procedure. The negative evidence afforded by a normal antitryptic index is of great value in excluding malignant disease.—B.M.J. ii./09,1220.

The electrical conductivity method is described. L. i./09,968. During a tryptic digestion the rise of electrical conductivity of the digest is an accurate



method of following the course of the reaction, and with it extremely small quantities of serum can be used.

The viscosity method depends on the changes of viscosity taking place during the process of digestion. Yields very reliable results.—B.M.J. ii./09 1058.

A raised antitryptic content often assists in distinguishing between an innocent neoplasm and a malignant one, but does not justify a positive diagnosis of cancer.—B.M.J. ii./09, 969.

In diagnosis of cancer of the stomach Hydrochloric Acid must be persistently absent from stomach contents—distinction from gastric ulcer and dyspepsia.—B.M.J. i./07, 746.

*Recognition of Cancer of the Stomach.*—Stress has been laid in the diagnosis of carcinoma of the stomach upon the *absence of free Hydrochloric Acid* and diminution of the total acidity of the gastric contents removed after a test meal—there are, however, so many exceptions that too great importance must not be attached to it. In chronic gastric ulcer and in carcinoma, originating in chronic ulcer free Hydrochloric Acid is usually present in about normal amount—sometimes slightly in excess, and the total acidity corresponds. In old standing cases with many years' history which may be chronic ulcer, or may have overstepped the line and become malignant, no information of value is given. In chronic gastric ulcer apart from growth very rarely, in carcinoma of other organs commonly, and after severe hæmorrhage, free Hydrochloric Acid may be absent. These exceptions to be borne in mind in considering the value of absence of free Hydrochloric Acid and diminution of total acidity.—B.M.J. i./11, 1458. *Vide* also pp. 279, 280.

**Oleic Acid method of diagnosis of Gastric Carcinoma.**—

The amount of Hübl's Iodine Solution, *vide* p. 73, necessary beyond the normal limits operating on gastric contents after a trial meal is taken to indicate presence of Oleic Acid. Out of 77 non-malignant cases it was only present twice, and in 22 undoubted cases of cancer the acid was present in all but one, in which there was marked gastrectasis.—B.M.J. ii./10, 1645—*ex Münch. Med. Woch.*, Sept. 20/1910.

Early diagnosis and treatment of cancer of the stomach. Evidence of impairment of the motor functions of the stomach, and of a diminution of the Chlorides in the gastric juice.—B.M.J. ii./10, 953.

**Reaction of the blood serum as aid in diagnosis of cancer**

Titration using Dinethylamido-azo-benzene as indicator. The results show that some sera are more alkaline to Dimethylamido-azo-benzene than others.—B.M.J. ii./13, 780.

**Abderhalden's Serum Reaction** has been used as diagnostic *q.v.*

Protozoan origin of tumours. The authors state they can demonstrate in many tumours bodies that are obviously protozoa, as also portions of a life cycle.—B.M.J. ii./09, 868.

Treatises on Protozoa.—*Na.*, Mar. 3/10, p. 1.—B.M.J. i./10, 142.

Possibility of a causal parasite cannot be denied. *Coccidia* theory not tenable. Actual results in treatment with Atoxyl—nil.—B.M.J. ii./03, 1509.

A real increase of cancer cannot be proved. The stomach is the seat of the disease in nearly 22% of the fatal cases in males in England and Wales. In females the generative and mammary organs are affected in more than  $\frac{2}{3}$  of the total cases. Whether cancer is transmissible by heredity in man has not been settled one way or the other. Importance of animal (mice) experiments being conducted under identical condition is emphasised. Old mice are not such good 'soil' for tumours as young ones. Animals can be rendered unsuitable for inoculation and growth of cancer by treating them with malignant new growths, or with normal tissues of their species. After exposure to **Radium** for an interval not long enough to cause any naked eye or microscopic alteration in the tissues, they may be completely deprived of their immunising or growing powers.

Cancer cells, even when of the same organ have been resolved into a larger number of varieties able to maintain the individuality than was previously conceivable. *No evidence has been obtained in favour of embryonic explanation of etiology, nor any analogy with known forms of infective disease.* At the present time the number of different kinds of tissues being propagated separately make it possible that the majority of the tissues, once they have acquired cancerous properties may be grown and segregated—in other words—a *living animal can be analysed into many of its component parts.*

Cancer is not limited to white men. 25,000 deaths annually from it in Japan. It is not, as usually supposed, rare in any quarter of the globe.

Old mice (and human beings) are more susceptible than the young. Location of the disease due to irritation is dwelt upon. Strong arguments against infective causation of the disease given. Mice and rat cancer distinct. Bashford, 16th Inter. Cong. of Medicine, Budapest.—L. ii./09,691; B.M.J. ii./09,797.

In inoperable cancer the **thyroid gland** has been *removed* as the best means of ameliorating the disturbing factor. There would seem to be increased thyroid activity in carcinomatous sufferers.—L. ii./09,1138.

Cancer, like all "new growth," must be regarded in the light of an adaptive response on the part of certain cells or cell groups to changes in their environments, and as the result of a process of variation and selection of an "inter" or "intra" cellular kind.—C. J. Bond.—L. ii./11,349,391. This article should be consulted for the author's deductions, also for statements of the theories of others on cancer.

Cancer in cuirasse.—Long considered due to a malignant infiltration of the lymphatics of the skin, but W. S. Handley says it is an œdematous infiltration of the tissues due to lymphatic blocking. A paper upholding the original view.—L. ii./11,356.

**IMMUNISATION BY RADIUM.**—If a portion of mouse carcinoma be exposed to Radium for a period of time insufficient to produce a structural change, and this fragment be subsequently inoculated into other mice, the inoculation fails, no growth takes place, but the same result may be obtained by other methods, *e.g.*, breaking up the fragments in a mortar, or heating to 98.6° F. for 24 hours. In mouse carcinoma already established by inoculation exposure to Radium causes some tumours to disappear, others go on normally. Sections from the disappearing tumours show hæmorrhage where the Radium had exercised its influence, but the most noticeable change is an active proliferation of the connective tissues, especially at the margin, and an invasion of the parenchyma of the tumours by young fibroblasts. These contract on, strangle and destroy, the epithelial cells they embrace. There is no evidence of a direct specific effect on the epithelium of the growth which is found to be still actively proliferating.—L. ii./10,291.

The therapeutic value of Radium consists in its employment to treat conditions other than cancerous ones—it has no selective effect. Surgical treatment the only way.—E. F. Bashford.—B.M.J. i./11,1221.

See also **Radium, Therapeutic Use of**, Vol. I., p. 690, *et seq.*

Chronic traumatic mastitis caused by **CORSETS** improperly made or worn. Cases are also frequently seen where the position of cancer in the breast corresponds exactly to the site of bone pressure of the stays. Patients should never wear anything that can act as a constant source of irritation, especially to epithelial tissue subject to such varying activity as that of the mammary gland.—G. L. Cheatele.—B.M.J. i./11,492.

**Local irritants** causing Cancer. Details of the causation of epithelioma by the carrying of the *cangri*, a portable fire basket, by natives of Kashmir; also details of pitch cancer, or fuel workers' cancer. Incidence of cancer amongst workmen engaged in making fuel briquettes.—B.M.J. ii./10,629; i./11,885. See also L. ii./10,1830.

Experiments with **air dried cancer pulp** showed the procedure is lethal to cancer cells. There is little evidence to show that cancer is an air-borne disease. Subcutaneous insertion of air-dried carcinoma produced no prophylactic immunisation to the growth of a subsequent graft, *i.e.*, that dead cancer tissue, whether killed by Radium or other means, was powerless as a prophylactic.—B.M.J. ii./10,1720.

**Nature and Origin of Cancer.**—Suggestion that the theory of extrinsic parasite explains the initiation of the cancer cell at the point of infection. The clinical history of the disease and successful experiment points to its extrinsic origin.—B.M.J. ii./11,1677.

Cancer a rich man's disease. The consumption of foods rich in Xanthin and Uric Acid produce gout and rheumatism and in producing them cause widespread irritation throughout the body.—B.M.J. ii./11,1678.

**Chemical irritants, Sulphurous Acid and Sulphuric**, also **Tar** have been held responsible for cancer.—B.M.J. ii./09,704,1215,1716.

**Sulphur** content in fuel in relation to cancer. Peat is found in



parts to be stronger in Sulphur than others and it appears cancer mortality is connected with high Sulphur content.—L. ii./13,506.

**Gasworks Pitch and Cancer.**—Men handling pitch or engaged in making briquettes occasionally suffer from warty growths which may ulcerate and become the seat of epitheliomatous cancer, or particles of pitch strike the eyes and induce severe inflammation of the conjunctiva and cornea which may end in loss of vision. H. C. Ross and J. W. Cropper investigated the chemical aspect of the problem.—B.M.J. i./13,36.

**Briquettes** and the incidence of cancer. It appears that the mischievous ingredient is some member of the Amidine group which distils at about the same temperature as Anthracene Oil, and is present in the rough Anthracene cake.—B.M.J. ii./13,506.

**Liquid Paraffin** is harmless and not likely to have any of the evils of pitch and tar in the cause of pitch cancer.—H. C. Ross and J. W. Cropper, B.M.J. ii./13,48.

**Genesis of cancer.** An enquiry showing cancer to be explainable as an essentially physiological tissue change not associated with any external cause, *e.g.*, parasite.—A. Turnbull, B.M.J. ii./13,905.

**Box**, of Montpellier, according to the Daily Press of 11/12/13, claims to have discovered the microbe of cancer. The parasite is stated to excite the cells of the body, causing them to proliferate rapidly in a typical manner. The organism is stated to be met with more particularly in water, especially stagnant water.

Cancer tissue cells are able to tear down the albumins of the body cell—in fact, to devour them. The reaction of the cancer cell is apparently acid, while the normal cell is alkaline—its chemical composition differs from that of the body cell. It is suggested that a substance may be found (*given per os*) that will have chemical affinity for the peculiar chemical constitution of the cancer cell. Cancer proteins exhibit a high content of Glutaminic Acid, Alanin, Phenylalanin and Aspartic Acids. The paper concludes, however, in praise of 'X' ray or Radium irradiation, combined with saturating the part with Anilin Dyes.—W. J. Morton, N.Y. Med. Jl., March 30th, 1912.

The late W. Forbes Ross held that cancer is due to want of balance in the mineral salts of the body. The intake of *Potassium* in particular, he held, was deficient owing to process of cooking and diet.

#### **Seventh International Congress of Medicine (1913—London).**

Cancer occurs in practically every phase of life and in every species as an indirect result of chronic irritation, but what the direct or actual cause of the disease may be is not known.—E. F. Bashford.

E. Freund (Vienna), stated that normal blood contains a substance which has the power of destroying cancer-cells. He had isolated the substance, a fatty acid which is soluble in ether and does not contain nitrogen. It is not present in the blood in carcinoma, but in its place is found a substance which possesses the faculty of destroying the normally present fatty acid. His theory is that the deficiency and disappearance of the fatty acid must occur in advance of, and not as a result of, the growth of a cancerous tumour.

Clowes (Buffalo) had found that the virulence of tumours and their rate of growth are directly proportionate to the potassium content and inversely proportionate to the calcium-content, *c.f.* Forbes Ross *antea*.

Minute quantities of Radium present in most tissues,—much increased in cancerous tissue. Examination of gallstones (always associated with cancer) showed that while a mere trace of Radium is to be found in them in non-cancerous cases, 85 times as much is present in cancer of the bladder, and even when the cancer was elsewhere than in the gall bladder there existed an increase of Radium in the gallstones.

Radium can be removed out of solution by *Staphylococcus Pyogenes Aureus*. Bacteria form the common foci of gallstones. Possibly bacteria concentrate the Radium around themselves and so form foci of gallstones thus leading to cancer of the gall bladder.—W.S. Lazarus Barlow,—L. ii./13,729,740 ; C.D. ii./13,357.

**Arsenic Cancer.**—Arsenic may well be one of many predisposing causes. A case described of a woman who had psoriasis treated by arsenic and who ultimately died of cancer, also a table of numerous allied cases.—L. ii./13 210,284.

**Uric Acid free diet** in inoperable cancer. Results of trials of a diet of nuts, fruit, biscuits, etc.—A. Haig, B.M.J. ii./12,81,150.

**Antimeristem.**—Stated to be a vaccine or Serum for the treatment of cancer. Various reports of a successful nature have appeared in German literature,—even in “hopeless cases.” The preparation is based on the theory of the parasitic origin of cancer. Has been employed in inoperable relapses and primary tumours, also to prevent relapses following radical operations and as diagnostic.

#### Coley's Fluid

Is prepared by cultivating the *Streptococcus* of erysipelas in bouillon ten days. *B. prodigiosus* is added, and the two are grown together for ten days. The culture is then killed at 60° C.

In Coley's experience of 500 cases there were only three deaths. Toxin treatment of inoperable cancer entitled to more careful consideration. *B. prodigiosus* has a curative effect on tumours, and intensifies the virulence of the toxins of erysipelas, hence a mixture of the toxins of this and the *streptococcus* employed.—L. ii./09,173.

The method was founded on the occurrence of retrogression in, and disappearance of, inoperable sarcomata as a sequel to attacks of erysipelas. Six weeks to three months treatment generally sufficient. 8 minim doses thrice weekly usually employed.—B.M.J. ii./09,144. See also Pr. Nov. '09,589 ; P.R.S.M. Surg. Sect., Nov. '09, p. 1 ; P.R.S.M. Clin. Sect. Mar. 1910, p. 114, Oph. Jan. 1911, p. 68 ; Coley, M.P.C. 1911,697.

The Lister Institute supplies 'New' Coley's Fluid (of red colour) in phials of 2 Cc. **Dose.**— $\frac{1}{4}$  minim at first, diluted with sterile distilled water, injected into the tumour or elsewhere, gradually increased until a temperature of 102 to 104° F. is produced.

Coley points out necessity of commencing with a small dose—a quarter of a minim—and the necessity of following this up by alternate local and *systemic* injections, also injections must be given until all reaction has calmed down and the temperature fallen.—M.P.C. i./12,31.

Melanotic sarcoma of the neck treated with Coley's Fluid injected in  $\frac{1}{2}$  minim doses increased to 3 minims, subsequently increased to 15 minims sometimes into the growth and sometimes into the chest wall.—B.M.J. i./12 19

Mixed-cell sarcoma treated locally, excision and Coley's Fluid  $\frac{1}{4}$  to 3 minim doses, successful.—B.M.J. ii./13,1484.

Fresh alarms on the increase of cancer.—E. F. Bashford, L. i./14,378.

For further methods of treatment of Cancer consult the **Therapeutic Index** — Vol. 1.

**Bacillus Coli Communis.** A normal inhabitant of the intestines, but becomes virulent in certain conditions. It increases the virulence of typhoid. The *Bacillus Coli* is present in an infant a few hours after birth. For further characteristics see *B. Typhosus* and Bacteriological Examination of Water.

**Bacteriology of Fæces.**—Bacteria in fæces which constitute about one-third of the dried weight are (a) digestive, and (b) antiputrefactive and



antiseptic. *B. Coli* is the chief bactericidal agent. It is destructive to nearly all bacteria except *Staphylococcus* and *Streptococcus*, and the other important defence is the intact intestinal mucosa. If either of these become defective, an enormous development of injurious and actively fermentative germs occurs, such as *B. acid. putrifici coli*, *B. liquefaciens*, etc. These, by their toxins and ferments, act upon the mucous membrane, destroying its continuity and giving rise to ulceration, creating a "vicious circle," the disease of the bowel altering the bacterial flora, and the bacteria increasing the ulceration; and the products of these secondary infections, when increased in amount, give rise to auto-intoxication with its accompanying constipation, headache, neurasthenia, etc., and in its later stages to arteriosclerosis and its attendant evils.—Pr.

Bacteriology of the alimentary canal,—an exhaustive treatise.—F. W. Andrewes, B.M.J. i./13,539.

Seven cases of cystitis in children shown to be caused by invasion of this organism.—B.M.J.E. ii./04,65.

Could not be found in London air. Desiccation necessary for it to gain access to the air, which is generally fatal to this organism.—Hewlett, L. i./09, 742.

BACILLURIA occurs with great frequency. 1. Associated with passage of pus: single abscess or more widespread infection of the urinary tract. 2. Milder stage—continuous passage of the bacilli but without pus or epithelial cells. 3. Intermittent passage of the bacilli. One often finds a history of constipation and a large proportion of cases are women.

In examining urine in which pus is absent one should note (a) Pale colour, paler than one would expect from the gravity. (b) Low acid reaction; rarely very acid. (c) The urine is hazy, not clear. Filter a little, if still cloudy, examine under the microscope: ( $\frac{1}{2}$  inch oil immersion). Round bodies or short rods (the former are the bacilli 'on end'). Note motility. Stain centrifugalised deposit by Gram's method. It is Gram negative. The urine should be fresh and collected in sterile flask by catheter if possible. Inoculate an agar tube with a large loop full—note opaque white growth after 24 hours with crenated margin. *B. Coli* isolated from the urine used to prepare vaccine. L. ii./09,1269—with revisions by Wyatt Wingrave.

Variability in the Gas-forming power of Intestinal Bacteria. It is possible to select a strain of *B. Coli* which fails to produce gas from certain Mono, Di-, and Poly-Saccharides.—P. R.S.M. Path. Sectn. 1911, p. 97.

*B. Coli* infections with reference to their recognition and comparative frequency:—

Accidental scalds on a child's buttocks developed diarrhoea, convulsions, temperature 104° F. Specimen of the fluid from the blisters on cultivation on Agar were found to yield pure growth of *B. Coli*,—infection being caused by child's motions. Cultures from the sputum and the urine of an anomalous febrile case gave a small bacillus, motile and—Gram staining. Fermented glucose and lactose with gas production; produced clotting and acidity in litmus milk. Production of Indol was not clear. There was no indication or stoppage of motility when the organisms were brought into contact with the patient's blood 10:1. The last negative result is not evidence of any great weight against the conclusion that the bacilli had a specific connection with the patient's illness. A mild coli and pneumo infection was diagnosed. In another case definite agglutination was obtained which coupled with + Indol reaction and other characters as above detailed, justified conclusion of *B. Coli* infection. Vaccine given.—B.M.J. ii./10,1301.

The **typical characters** of *B. Coli Communis* are as follows:—

1. The formation of Indol in broth culture—identified by the intense redness produced by Ehrlich's Rosindol Reaction, *Syn.* Böhme's Indol Test—addition of Paradimethyl-Amido-Benzaldehyde (1% solution in Absolute Alcohol and Hydrochloric Acid) and Saturated Solution of Potassium Persulphate. To conduct this test, see Bact. Examination of Water, p. 257.

2. The coagulation and acidifying of Litmus Milk.

3. The acidifying of McConkey's Fluid with gas formation.

4. The reduction of neutral red to yellow fluorescence.

5. The growth of red colonies on Conradi-Drigalski's Medium (see p. 253).

6. The formation of gas in glucose gelatin 'Shake' culture at 22 C.° without liquefaction of the gelatin.—B.M.J. ii./10 1133.

Specific differences amongst bacteria. The varieties of *B. Coli* are almost infinite.—L. ii./13,1241.

The presence of anaerobic bacteria is believed to account for abnormal putrefaction in the intestine—normally the bacteria are either aerobic or facultative anaerobes—mainly whilst the anaerobic are in the minority. Excess of the anaerobic bacteria may be caused by excess of animal food,—auto-intoxication can undoubtedly be traced to this. Again the food may be excessively contaminated with bacteria, *e.g.*, in pyorrhœa alveolaris, and post-nasal catarrh. Further, it may pass from the stomach imperfectly digested. There is in addition purely intestinal putrefaction. One of the agencies of defence by nature against such injury is the combating of toxins by the intestinal flora—principally *B. Coli*—this organism is furthermore stated to produce thermolabile and thermostable substances which not only inhibit the growth of other organisms, but also their own if given long enough time to act.

Diagnosis of abnormal putrefaction may be assisted by estimating (1) URINE, increase in ethereal sulphates in the urine; increase in total output of aromatic bodies; rise in capillary constant; examination for Indican and other constituents. (2) EXAMINATION OF THE FÆCES,—staining by Gram's method and counterstaining with neutral red—the *red organisms should preponderate* (*B. Coli* is non Gram Staining). In abnormal putrefaction in proportion as the aerobic bacilli are replaced by strict anaerobes (mostly + Gram) the blue stained will be in excess. A loopful of a 1 in 100 suspension of fæces in sterile milk should not produce a rapid gas formation (*e.g.*, by *B. Aerogenes Capsulatus*).—G. Herschell.

*B. Coli* in urine is sometimes seen joined end to end forming a spirillum-like structure. It will grow both in urine rendered artificially many times more acid than normal, also in alkaline urine—*more readily in acid*.—A Jordan, B.M.J. ii./13,649.

BACILLURIA AND PYURIA.—Estimate the Acid Index by titrating 10 Cc. of the urine with N/10 Sodium Nitrate using Phenolphthalein. If low, administer Acid Sodium Phosphate thrice daily in order to increase the acidity up to even 10° and to keep it up. Albumin (due to Globulin probably due to Leucocytes) may be found, also Acetone.

The chief bacteria concerned are *B. Coli*, *Streptococci* of the long type, which are more feebly Gram + than *St. Pyogenes*, *Staphylococcal forms*, and "Beaded" bacilli of the *B. Xerosis* type, further a great variety resembling *B. proteus vulgaris*.

All of these have been found in bacilluria with joint troubles, but the most striking cases afforded almost pure culture of streptococcal form. They closely resemble the *streptococcus salivarius*, a common inhabitant of the throat. Tubercle bacilli should always be looked for, especially if lymphocytes are present. Pneumococci are said to occur, but in connection with acute cases, while gonococci play an important role by themselves.—Wyatt Wingrave, Pr. Dec. 1912.

*B. Coli* will grow equally luxuriantly in either alkaline or acid urine.—L. ii./12,1208.

For the effect of Formaldehyde upon this organism (*i.e.*, on treatment with Hexamethylenetetramine and Sodium Acid Phosphate), see our investigation, p. 67 and 68.

B. COLI IN THE BLOOD.—Blood cultures made from persons suffering from undoubted Coli infections are almost invariably sterile. On three occasions pure growths of the bacillus were obtained from the blood. In two cases they were obtained whilst patients were actually suffering from a rigor and in the third 3½ hours after a rigor.—L. ii./12,1500.

For **Musgrave's Medium** for cultivating *B. Coli*, see Culture Media.

For *Distinction and Separation from B. Typhosus* vide Bact. Examination of Water and *B. Typhosus*.

**Bacillus Diphtheriæ.**—The latest work leads to the opinion that this organism is of the nature of a Streptothrix). *Directions for collecting specimens.*—If a sterile swab is not at hand (which should be used with aid of a tongue depressor), a small piece of absorbent cotton wool (not medicated with an antiseptic) should be steamed, *e.g.*, at the mouth of a kettle, allowed to cool and rubbed over the membrane on the fauces of the patient and removed in a test tube or bottle which has been similarly sterilised. If possible a small portion of the membrane should be detached in addition. The organism may persist for many months in nasal and aural discharges.



The organism in dry condition and in the absence of light has been shown to persist for many months, an important point to recollect in disinfection of bed linen. Moist heat destroys the organism rapidly, *e.g.*, a temperature of 60° C. Is also very sensitive to treatment by antiseptics. Nurses in charge of patients should be examined occasionally as the organism may be present without symptoms of illness and infection by such agency should be guarded against. An injection of Antitoxin is a safeguard.

**Films** are prepared from the swab. Stain with Borax Blue, counterstain with Vesuvine or by Gram's method (Gram+). Dry and mount in xylol balsam.

**Recognition.**—*B. diphtheriæ* may be distinguished from the other organism, which will probably be seen in large numbers by the following characteristics—Irregularity in size and outline, straight or slightly curved, more or less clubbed at one or both ends (clubs chiefly in cultures), sometimes spindle shaped, or as curved wedges, occasionally irregularly segmented, rarely or never regular in outline. Parallel grouping and 'Chinese alphabet' characteristic. Stain irregularly. Show irregular beading with Borax Blue and Vesuvine, which is the best stain to demonstrate the granules—and Gram's method, *v.p.* 361. **Cultivate on blood-serum**—fine cream-coloured growth in twelve to sixteen hours, film from the same stain with methylene blue, Neisser's or Gram's method. Cultivations should in all cases be made on blood-serum or glycerin agar before the result of diagnosis can be positive. Further characteristics,—no spores, non-motile. Form differs with culture medium.

**Neisser's original method** of staining the organism:—

Stain  $\frac{1}{2}$  minute each (washing between with water) with

A. Methylene blue, 0.5 Gm.

Alcohol absolute, 10 Cc.

Distilled water, 475 Cc.

Glacial acetic acid, 25 Cc.

B. Bismarck brown, *syn.* Vesuvine  $C_6H_4NH_2.N_2.C_6H_3(NH_2)_2.2HCl$ , 1 Gm.

Distilled water, 500 Cc.

but altered in the length of time [which was 3 seconds with A. and 10 seconds with B. (B.M.J. i./03,587) to 2 minutes each], advocated for examining direct from the swab.—B.M.J. ii./01,758.

The use of Eosin Solution instead of B. above gives good results, working as follows:—

1. Make film in usual manner. 2. Stain with A. three minutes, and without washing pour on Gram's iodine solution 1 minute. 3. Wash in water and counterstain with eosin 5% aqueous solution 3 minutes, wash dry and mount. This method was claimed to be diagnostic, but other organisms, *e.g.*, *B. Xerosis*, *B. Proteus Zenkeri*, *B. Cyanogenus*, and various organisms found in water, give similar results. The granules are stained blue, the rest of the bacillus is stained by the counterstain.

Good results direct from the swab are obtained by the following:—Stain with Alkaline Methylene Blue (*v. p.* 344) 3 to 4 seconds, afterwards with B. above.—L. i./03,92.

**Toluidin Blue Stain for**—Toluidin Blue 0.02 Gm., Glacial Acetic Acid 1.0 Cc., Absolute Alcohol 2 Cc., Water to 100 Cc. A loopful of the Stain is dabbed on the dried smear and examined as hanging drop with 1/12th inch oil immersion lens. Used for direct examination from the swab, the appearance is characteristic. *B. Diphtheriæ* appears pale blue with bright and often deeply stained red granules along its entire length, some yeasts and sarcinæ also show the metachromatic markings. Hoffman's bacillus stains dark blue with a light band. Diphtheroid bacilli cannot be mistaken or confused with *B. Diphtheriæ* by the method. It would be well to make the film, if possible, direct from the throat. A negative result is not to be considered of much value. Vincent's angina fuiform bacilli also stain dark blue. The method is claimed to be simple and rapid.—Constant Ponder, L. ii./12,23.

Two reputed pseudo-varieties; one morphologically and in all respects similar to the specific organism, but non-virulent, the other of **Hofmann** shortly after the latter—stains more regularly than the diphtheria bacillus, and usually shows no polar staining. Uniform in shape, size and staining.

The general trend of opinion is that the *Hofmann Bacillus* is quite distinct but Hewlett thinks that the *Hofmann Bacillus* really includes several species

of which one may be a modified form of the diphtheria bacillus.—B.M.J. i./12,75.

**Morphology** of the bacillus varies greatly. From different individuals one may obtain (a) uniformly cylindrical bacilli with deeply staining round or oval terminal granules and the rod varying in length, or (b) very irregular in size and staining, and may be slightly curved. Further there seems to be *seasonal prevalence*; thus the *cylindrical* form, while it may prevail throughout the year appears to *predominate in winter* and be *irregular in summer*.

The importance of bacteriological investigation in the case of the diphtheria Bacillus.—L. i./12,224.

### **Pathogenicity of true Diphtheria Bacillus compared with pseudo forms.**

Five Cc. of a glucose-broth culture two days old with pseudo-diphtheria bacilli are not pathogenic to guinea-pigs, whereas  $\frac{1}{2}$  Cc. of a similar culture of true diphtheria bacilli usually kills in two days.

**Glucose Litmus Broth** cultures of true diphtheria bacilli show marked acidity in 24 hours, while those of the pseudo forms are stated not to evince this alteration of reaction. *This method is useful for confirmation where no licence for inoculation of animals is held.*

**Serum water** gives good result:—

Coagulate blood serum in an equal quantity of water, filter, add to one half 1% glucose, and to the other 1% Saccharose. Add neutral red as indicator. After 24 hours a marked acid is produced in the glucose tube by *B. diphtheriæ* in both the glucose and the saccharose tubes by *B. Xerosis* (*vide infra*) and no change is produced in either tube by Hofmann's Bacillus.—B.M.J. ii./09, 520.

*B. Paralyticans longus* and *B. paralyticans brevis* (Muirhead's Diphtheroid Bacillus) have been isolated and studied.—L. ii./08,1438.

**B. Xerosis** occurring in xerosis conjunctivæ also in nose, throat and ear, differs in the fact that primary cultures from the eye on blood serum first appear in 36 hours. Sub-cultures do not show this difference. The organism is non-pathogenic to guinea-pigs.

Characters. Gram + and very similar to *B. diphtheriæ*; often occurs in the throat.

**Koch-Weeks bacillus**, a thin, non-motile organism decolourised by Gram's method, is found in a large number of cases of conjunctivitis. A diplo-bacillus has also been found which causes an extremely dangerous form of conjunctivitis, but it is amenable to treatment.

**B. Morax-Axenfeld**.—Angular conjunctivitis is the only form of conjunctivitis in which the clinical appearance is characteristic of the organism at work.—the diplobacillus of Morax-Axenfeld (Gram-). Boric lotion and Zinc Sulphate 0.5% rapidly effects cure.—B.M.J. i./09,1221. A serum is not worth the trouble of preparing.—Axenfeld, B.M.J. ii./08,738.

**Potassium Sulphocyanide Medium** for differentiation of *B. Diphtheriæ* and associated organisms,—Potassium Sulphocyanide 1, Calcium Chloride 1, 1% Aqueous Neutral Red Solution  $\frac{1}{4}$ . Glucose  $\frac{1}{2}$ , Broth 25, Sheep's Serum 75, adjusted so that on coagulation the reaction is faintly alkaline. Found of service for the routine recognition of *B. Diphtheriæ*, *B. Hofmanni*, *Torulae*, *Micrococci* and *B. Subtilis* by subcultures. Colonies of *B. Diphtheriæ* almost invariably a bluish pink tint with diffusion of the tint through the medium.—Jl. Path. and Bact., July, 1911,130. The following Media are on similar lines:—

To Sheep's Blood Serum to which has already been added 1% Glucose and 1% of  $\frac{1}{2}$ % Solution Neutral Red indicator (this preliminary combination being denoted as "S") there is added either singly or in combination one or more of the following:—

(A). Potassium Sulphocyanide 1%. (B). Potassium Ferrocyanide 2½% (C). Potassium Ferricyanide 1% (D). Boric Acid 1%.

The Medium on coagulation and inspissation should be faint primrose-yellow in colour and faintly alkaline. The Sheep's Serum is best pipetted off from recently drawn clotted blood and then allowed to stand in a refrigerator for three days in order to eliminate red corpuscles by sedimentation, only the supernatant liquid being finally utilised. With combination 'S.A.' *B. Diphtheriæ* grows red with a bluish-pink tint diffusing through the medium in all



directions; *B. Hofmann* grows yellow with yellowish diffusion. Some varieties of *Staphylococci* simulate *B. Diphtheriæ* on culture, but on further incubation the tint does not intensify as with *B. Diphtheriæ*, and should be readily distinguished; *B. Subtilis* grows brownish, *B. Megatherium* and *Torulae* grows as faint pinkish-white colonies, which are raised; *Streptococci* grows apparently colourless. Combinations 'S.A.B.' 'S.B.' and 'S.D.' in particular show up to advantage the reddening and bluish-pink diffusion brought about by *B. Diphtheriæ* as compared with various *Staphylococci*. The general rule may be taken as "No red coloration no *B. Diphtheriæ*." This coloration may be seen with the naked eye and hence has advantage for rapidly identifying subcultures from swabs of suspicious nose and throat cases.—B.M.J. i./ii,759.

### Potassium Tellurate Culture Medium.

Meat Extract 10 Gm., Salt 5 Gm., Witte's Peptone 20 Gm., Acid Calcium Malate 6 Gm., to 1,000 Cc. of Water. Heat for half an hour and filter, and add 1% Glucose and three times its volume of Sterile Ox Serum. To each 100 Cc. of the mixture 2 Cc. of a 1% Potassium Tellurate solution are added and the result poured into a Petri dish and coagulated by heat. The material to be examined is first incubated for three hours on Blood Serum, after which the plates thus prepared are inoculated from the cultures thus obtained. The diphtheria bacillus has the power of converting the tellurium salt into tellurium dioxide, which stains the colony black; pseudo-diphtheria bacilli form colonies of a grey colour, whilst those of staphylococci are brown. Most other organisms grow badly in this medium.—Conradi and Troch, Munch. Med. Woch., Vol. LIX., p. 1,652. Pr. Feb. 1913.

**Sections of Membrane.**—Stain for the diphtheria bacillus by the Eosin-Gram method:—

1. Stain 4 or 5 min. with eosin solution. 2. Wash well in water. 3. Pass through a little alcohol. 4. Stain with anilin-gentian-violet, 10 min. 5. Cover with Gram's iodine solution, 3 min. 6. Decolorise with anilin oil. 7. Clear with xylol and mount in xylol balsam.

**Roux's Stain for Bacteria.**—Dahlia or Gentian Violet 0.5 Gm., Methyl Green 1.5 Gm., Distilled Water 200 Gm.

Diphtheria organisms in throats of insane.—L. ii./05,465.

Diphtheroid organisms found in respiratory tracts in many cases of tabes dorsalis, but they cannot be proved to cause the tabetic toxin.—L. i./06,954.

### Diphtheria Antitoxin, Serum Antidiphthericum, U.S.

#### Preparation of Diphtheria Antitoxin.

Consists of the fluid separated from coagulated blood of the horse immunised by inoculation with diphtheric toxin, produced by the filtered culture of the *Bacillus diphtheriæ* in broth—a surface growth is important. Repeated injections during 4 to 6 months of increasing quantities of toxin up to as much as  $\frac{1}{2}$  or 1 litre render the serum of a high antitoxic quality. When the horse's serum reaches the stage at which a combined injection into a guinea-pig of serum *plus* a dose of toxin leads to no symptoms of diphtheria, it is considered to have attained the required potency. The horse is bled about 10 days after the last injection and the serum prepared for use as a remedy, and as a prophylactic.

That of P. Belg. and P. Jap. must be marked with the name of the maker, date, and rotation number, also the number of units per Cc. in the vial. Keep in the dark in a cool place. P. Jap. states the serum must be sterile. This pharmacopœia has:—

(A) *Serum Antidiphthericum Liquidum*, which should possess not less than 500 units in 1 Cc. Three Classes—No. 1 contains 600 antitoxic units; No. 2, 1,000 a. units; No. 3, 1,500 units. Injected subcutaneously, 0.5 Cc. should not kill a mouse of 15 Gm. weight, nor should 10 Cc. be fatal to a guinea-pig. (B) *Serum Antidiphthericum Siccum* 1 Gm. represents at least 5,000 antitoxic units.

#### Units of Immunity.

The E. B. Unit refers to the toxin neutralising power of the serum, not to the volume of the liquid. A normal serum is prepared for comparative purposes; 1 Cc. of this contains 1 unit of immunity, and 0.1 Cc. of it neutralises 1 Cc. of normal standard toxin.

The strength of sera is ascertained by physiological tests on guinea-pigs

weighing, as near as possible, 250 Gm., using mixtures of different quantities of the serum, and a lethal test dose of standardised toxin. The neutralising point is indicated by the animal's death being prevented on the fourth day.—For further details consult Hewlett, P.J. ii./04,377.

**Preservation.**—Experiments in U.S. started in 1906 by J. F. Anderson of the U.S. Hygienic Laboratory showed that there is marked loss in antitoxic value on standing at room temperature,—e.g., in 2 years a loss of over 30%. Dr. Anderson finds that dried diphtheria antitoxin keeps in darkness at 5° C. with its potency unimpaired for at least five-and-a-half years.

### *References to the use of Diphtheria Antitoxin.*

The earliest report of the use of the antitoxic serum is found in the Deut. Med. Woch. of April 27, 1893; this is noted in B.M.J. i./93,83. Behring and Kossel were the investigators; they give notes of 30 cases of diphtheria, so treated, of which 24 recovered, or 80%.

First English reported case by Eastes, 5 Cc. of Aronson's preparation in a child of 10 years, with recovery.—B.M.J. ii./94,125. Second,—p.180.

Post-diphtheritic paralysis is said to have been on the increase since introduction of antitoxin treatment, but this is not proper hoc. Antitoxin has, on the contrary, some power in restraining. Does not, however, neutralise the toxic material causing paralysis.—Bosanquet.

Diphtheria attacked a wound and produced death by systemic poisoning.—L. i./05,1130.

In nasal diphtheria, large doses of antitoxin are called for.—Bosanquet p. 98.

Saline injection as an adjuvant.—L. ii./01,1131.

Diphtheria bacilli found in suppuration of the scalp, also in vulvitis and in the pus in empyema, also in the pus from a breast abscess.—B.M.J. ii./07, 493.

Diphtheria of the skin—the primary seat of infection being the eyes—thence to the vulva and the lower part of the face, satisfactorily treated with antitoxin.—L. i./08,15.

In erysipelas in some cases the injection of Diphtheria Antitoxin causes rapid fall of temperature with disappearance of skin manifestations.—Pres. Nov. 1911, p. 285,—ex Klin. Therap. Wochen. April 24, 1911.

Diphtheria, malignant with multiple lesions in a child six weeks old failed to respond to 12,000 units of Antitoxin. Of 7,285 cases only 76 (1.04%) were under one year.—P.R.S.M. Diseases of Children Sect.—Feb. 1910, p. 74.

In ocular diphtheria 2 injections (2,000 to 10,000 units) adequate,—a third or fourth may be necessary.—Oph. Jan., 1911, 70, 694.

Epidemiology, diphtheritis is exceedingly common amongst pigeons.—L. ii./08,1143.

Pigeon diphtheria has nothing to do with human diphtheria.—Na. Mar. 1911, p. 117.

In diphtheritic conjunctivitis must be used early. If no response a mixed infection may be present.—Axenfeld, B.M.J. ii./08,737.

1,550 cases of diphtheria—78 of which (5 %) were hæmorrhagic—treated with high doses of Antitoxin. As a rule not more than 1 injection daily,—the maximum at one time rarely exceeding 24,000 units. Subcutaneously preferred. Adrenalin given internally.—M.P. Oct. 1909 390.

### **Oral and Rectal Use of Antitoxin.**

Should *not* be given *per anum* or *per os*.—Hewlett, Lecture on Antitoxins P.J. ii./04,888, faith in oral administration.—B.M.J. i./06,379. Doubt as to conclusions to be drawn.—B.M.J. i./06,738.

In quinsy or bad scarlet fever throats,—per rectum useful.—L. i./99,1636.

Antistreptococcic Serum in diphtheria is as efficacious given per rectum as hypodermically.—B.M.J. i./07,20.

Diphtheria Antitoxin given by the mouth thought to have specific action and may be advisable in certain circumstances.—B.M.J. i./11,494.

Diphtheria Antitoxin *per os*. Surer results are obtained when given hypodermically.—B.M.J. ii./11,1235.

Serum by the mouth,—smaller dose than hypodermic, 2,000 units, followed up, if necessary, by a further dose.—B.M.J. ii./11,108.

In local tuberculous diseases and in several cases of phthisis stated to have proved of value.—B.M.J. i./07,20.

Cupric Ionisation, *vide* Iontophoresis, has been employed in case of local chronic diphtheria of the ears.—B.M.J. ii./09,519.



Latent diphtheria treated by Vaccines.—B.M.J. ii./09,519.

Boils and septic conditions in young children have been well treated by Diphtheritic Serum. Specific characters of Sera doubted, effect thought to be due possibly to a by-product.—a nuclein derivative,—in the serum. Asthma has also been benefited,—dose given 1,000 units repeated at intervals.—Aikman, Guernsey.—B.M.J. ii./09,1016.

In diphtheria the use of Alcohol which used to be taught as imperative owing to frequency of heart failure has been found to interfere with the acquirement of immunity, also that in diphtheria heart failure is due to nerve degeneration caused by the diphtheria toxin, therefore Alcohol is contra-indicated. Antitoxin was freely given—there were 11 deaths in 114 cases.—L. ii./11,110.

Diphtheria,—two unusual cases. After childbirth a woman had a parotid abscess in which *Staphylococci* were found. Later the voice became husky, there was respiratory stridor, and she died. Post mortem,—a diphtheritic membrane in which *B. diphtheriae* was found extended from the vocal cords to below the bifurcation of the trachea. The other case was a nurse who had attended a bad case of septicæmia. Patient developed high temperature and great cyanosis and failure of strength. *B. diphtheriae* was found in sputum, etc., without ordinary clinical signs of diphtheria. Serum was of no avail.—L. i./13,691.

### UNTOWARD RESULTS, SERUM RASHES, ETC., WITH DIPHTHERIA ANTITOXIN.

Sudden death following injection.—B.M.J. i./02,1025.

Hypersensitiveness to 1,000 units injected for prophylaxis.—B.M.J. i./08,147,925.

A case in which 3,000 units of serum were injected, and in less than 10 minutes patient's eyelids began to swell, involving the whole in less than an hour. Lips thickened and the whole body was covered with an urticarial eruption. 20 grain doses of Calcium Chloride every 2 hours—swelling disappeared in 14 days.—B.M.J. ii./09,95.

Calcium Salts as prophylactic against serum rashes.—L. ii./11,1694.

Untoward results (Leader) following antitoxin.—L. ii./08,749.

Should be administered with great caution to asthmatic patients, even as prophylactic.—B.M.J. ii./09,356.

Serum disease is a familiar example of increased susceptibility or anaphylaxis.—L. i./11,594,

Anaphylaxis to Diphtheria Antitoxin.—Intense itching, subsequently vomiting, cured by  $\frac{1}{2}$  grain Morphine.—B.M.J. i./11,495.

Serum rashes and Serum sickness in diphtheria, *i.e.*, following the hypodermic injection of Diphtheria Antitoxin and other sera are said to be modified by simultaneous use of Thyroid Gland—up to five years  $1\frac{1}{2}$  grains daily for six doses, from 10–15 years and upwards 5 grains on alternate days for 4 doses. Out of 100 cases 16 suffered Serum sickness who did not receive Thyroid, whilst only 6 suffered who received it.—L. i./11,373.

Though the Serum is specific it must be used early, and there are limitations to its use.

The symptoms of Diphtheria Serum Sickness are fever, rash, usually urticaria or a variety of erythema multiforme occurs in about 33% of cases treated, sometimes more unpleasant effects, namely, pains in joints, tendons and fasciæ with fever. Result of observations is that the use of Antitoxin as a prophylactic is not approved of. Indiscriminate use unjustifiable.

Infective endocarditis well treated by Antidiphtherial Serum.—B.M.J. i./10,14. Protective Inoculation in Diphtheria Epidemics.—M.P.C. ii./11,429.

Profuse hæmorrhage in diphtheria.—A case of a boy aged five treated by severa 4,000 units of Antitoxin by the mouth, in addition injections of 2,000 and 4,000 units. At the time during the case about  $1\frac{1}{2}$  pints of blood were passed with membranous casts. One piece more than 2 ft. long. The *prima via* was clearly implicated and the topical use of the Antitoxin was successful.—W. F. Clark, B.M.J. ii./13,1484.

DIPHTHERIA CARRIERS are found of all ages and of either sex, the presence or absence of an obvious pathological condition is no criterion for detecting a carrier, of the length of carrier life, or of virulence. The length of carrier life seems to have no effect on virulence,—bacilli have been demonstrated to be virulent after four and eight months in the ear and nose of different individuals. The transference from animal to human is rare. Further

prosecution of work may result in finding harmless organisms where implantation and growth on diphtheria-infected persons may result in ousting the bacillus diphtheriæ from its usual haunts.—L. i./11,795. See also B.M.J. ii./10,1508.

The length of carrier-life of the bacillus appears to have no effect upon its virulence since the organism has been proved to be virulent after four and eight months in the ear and nose. A. Graham Macdonald outlines his scheme for dealing with the disease.—L. i./12,662.

**Dysentery.**—There are two main types of dysentery—Amœbic and Bacillary (c.f. *Vol I.*, p 486).

**To search Stools and Mucus for Amœbæ.**

In searching mucus for amœbæ stain with a little Methylene Blue and examine with low power, e.g.,  $\frac{1}{2}$  inch—turn on the  $\frac{1}{4}$  inch to verify. It has been said it is important to differentiate between *Amœba Coli* and *A. hystolytica*. Rogers states this is unnecessary, as *Amœba Coli* occurs very seldom.—L. ii./12,1064.

Alternatively,—place a small piece of freshly passed stool on a slide, adding one or two drops of 1 in 10,000 Neutral Red in Normal Saline. Examine with  $\frac{1}{6}$ th inch objective. The Amœbæ take up the Neutral Red,—all other constituents of the fæces,—even the leucocytes—remaining uncoloured.—Sir C. P. Lukis, B.M.J. i./13, 1357.

**Bacillus Dysenteriæ.** In our last Edition we gave numerous abstracts and references to work on the bacteriology of dysentery. The position is, however, by no means clear, there has been, it appears, renaming of identical bacteria. It will be best to state the opinion of Muir and Ritchie on the subject, which is to the effect that the bacteria of dysentery are divisible into two main groups, i.e., the Shiga-Kruse group and the Flexner group,—there are intermediate forms. The Shiga group does not ferment Maltose or Mannite, and, generally speaking, does not produce Indol, while the Flexner group does both. Neither of the groups produce changes in Saccharose or Lactose.

American writers regard all the various strains as of equal etiological importance, while the Germans hold that the Shiga-Kruse Bacillus is the only true type.—Sir C. P. Lukis, B.M.J. i./13, 1357. For further abstract of this paper see Vol. I., p. 486.

The bacilli of Shiga and Flexner are non-motile, non-sporing, and do not stain by Gram's method and grow on all ordinary media. In cultural characters they resemble *B. coli communis*.

Shiga's Bacillus isolated in 26 cases of dysentery in S. Africa out of 55 examined.—B.M.J. i./06,680; L. i./06,904.

Epidemic sporadic dysentery traced to Shiga's Bacillus.—B.M.J. i./06,1325.

Summer diarrhoea of infants. A number of Bacilli isolated from the stools.—B.M.J. Apl. 21/06; B.M.J. ii./07,16.

Epidemic diarrhoea in this country caused by a dysentery organism.—B.M.J. i./09,1227.

Flies as carriers of micro-organisms resulting in infantile dysentery. Muslin to be kept stretched over the child's milk.—L. ii./08,715.

The close relation of the prevalence of infantile diarrhoea mortality and the prevalence of flies is shown in a number of diagrams of plotted curves which are wonderfully coincident. Insect porters of bacterial infection.—C. J. Martin, L. i./13,1,81.

The two varieties of Shiga and Flexner certainly account for the dysentery of Japan, China, the Phillippines and the West Indies. One or other occasion-



ally appears in temperate countries. B. Dysenteriae is difficult to isolate.—B.M.J. i./09,768.

At least seven different dysenteries to deal with at El Tor among Mussulman pilgrims.—B.M.J. ii./09,862.

**DYSENTERY CARRIERS.**—Healthy carriers are very rare and of no importance. Actual carriers are to be found among the incomplete convalescents which form a high percentage of the cases. In combatting an epidemic it is necessary to reduce as far as possible the number of such cases and to isolate very strictly those that are already of this type.—B.M.J. ii./10,1507.

Isolation of pure dysentery toxin has been effected by Kirschbaum and Fränkel by means of an ultrafilter, *i.e.*, filter-paper that has been impregnated with Acetic Acid Collodion under pressure of six atmospheres. The toxin is a colloidal body kept back by the filter, it is poisonous and alkaline,—the filtrate is non-poisonous—its toxicity and immunising power is neutralised by acids, but restored again on adding alkali. The substance which has been separated from a broth culture of the Shiga-Kruse Bacillus is not identical with nucleo-protein. The presence of Sulphur, Purin or Carbohydrate could not be demonstrated. One decigram sufficed to kill a rabbit.—M.P.C. i./14,394.

A review of knowledge of dysentery to date.—F. M. Sandwith, L. ii./14,637,683,783.

**Bacillus Equi.**—Pathogenic for rodents. In horse blood.—Klein, L.i./06,782.

**Filaria.**—In *Filaria sanguinis hominis*, or elephantiasis, there are two kinds, nocturnal and diurnal, which only appear in the blood immediately below the skin at night and day respectively, and the mosquitoes, in which the cycle of the parasite's existence is completed, only bite during these respective periods. An effective treatment, therefore, is to alter the patient's sleeping period—*e.g.*, by keeping him awake at night.—Cantlie. The parasite is acquired by drinking infected and polluted water. Larvæ only of *Filaria nocturna* occur in the blood. The worm itself is subcutaneous. Elephantiasis in all its phases is very marked in these localities. The worm is introduced under the skin in early stages by the proboscis of a type of *Culex*.

The female adult worm was discovered by Bancroft, the male by Aranjo, and the embryo by Demarquay and Lewis. The embryos inhabit the lymph channels of the lower extremities and the scrotum. They lead to dilatation of the lymphatics, to hyperplasia of the tissues, chyluria, hæmaturia, abscesses, &c. They are found in the blood at night.—Gould.

Eosinophilia in filarial disease. The eosinophile cells accumulate round the encapsuled fluke.—L. i./06,1623.

A tick, *Ornithodoros Moubata* (Murray) is probably the intermediate host of *Filaria*.—B.M.J. i./07,143.

Prospective cure for elephantiasis by introducing silk threads into the limbs to replace the trunk lymphatics, and thus remove fluid from the œdematous part.—L. i./09,31. Palliative treatment by Thiosinamin, with bandaging.—B.M.J. ii./08,1361.

Filariasis Discussion opened by G. C. Low.—B.M.J. ii./13,1299.

**Micrococcus Gonorrhœæ.**—Stain first specimen by Gram's method, second by Acid Thionin, third by Pappenheim's Stain, or alkaline methylenes blue 3 to 5 minutes, wash in water, dry and mount.

#### RECOGNITION:

A medium sized diplococcus; reniform in shape, in groups, intracellular character, thought to be of no value in differential diagnosis, though previously stated to be so, but *vide* M. and R. The organism is Gram negative.

**Culture.**—Blood agar; difficult to grow; slow growth, small discrete "dew drops."

**Milk Serum (Sabouraud & Noiré).**—A new culture medium for gonococcus—to replace the use of Ascitic fluid—as in **Nasgar Medium**, see Abel and Gordon's Bacteriology, p. 147—which is both difficult to obtain and sterilise at a moment's notice.

(1) A litre of fresh milk is boiled for five minutes; (2) the Casein is then precipitated with 2 Cc. of Hydrochloric Acid, and the Serum recovered by simple passage through a piece of linen; (3) the filtrate is then added to half its quantity of water and the mixture neutralised with 10% Soda Solution;

(4) it is then autoclaved at 120° for ten minutes; (5) the following are then added in the strength indicated: Peptone 1 in 100, Glucose 1 in 100, Urea 0.3 in 100, Agar 1.6 in 100; (6) filtration and division into separate test-tubes, which are sterilised for ten minutes at 110° C., completes the preparation.—B.M.J.E. ii./13,44.

Isolation of gonococci may be effected from the fluid of gonococcic arthritic joints. It is not easy to obtain the gonococcus from the blood, although cultures are often obtained therefrom; when urethritis has ceased and fluids have disappeared from the joints, one proceeds by drawing 2 Cc. of the blood, with aseptic precaution, from the median basilic vein, and mixing with double the quantity of Agar Agar and plating immediately.—W. Murrell Pr. Jan. 12, p. 35.

#### Milk Broth or Milk Agar for cultivation of *Gonococcus*.

Fresh Milk 1,000 Cc. is mixed with 5 Cc. of 1 in 4 Hydrochloric Acid and kept at 37° C. for 16 to 20 hours to precipitate Casein, or the milk can be boiled, filtered and the filtrate neutralised with 10% Sodium Hydrate—then place in autoclave 2 hours, boil, neutralise again and filter. The filtrate is mixed with equal parts of broth, or one or two parts of 'Agar.' Put into test tubes and sterilise.—J. E. R. McDonagh, Pr., Nov./10.

**Pyronin Stain, Syn. Pappenheim's or Unna's Stain.**—Concentrated Aqueous Pyronin Solution 1, Concentrated Methyl Green Solution 3, is useful. Stain 5 minutes, wash and dry. Gonococci stain red, cells, etc., blue.

Wyatt Wingrave's Modification = Pyronin (water soluble) 2, Methyl Green 3, Distilled Water 100. Dissolve separately, mix and filter. After staining, wash with water and differentiate with 5% Resorcin in Alcohol.

All organisms by this method, especially the Gonococci, stain a brilliant red and pus cells greenish-blue. The Gonococci are found in regular clumps of Diplococci, the distance between each pair being much the same. Some are intracellular.

The diplococcus can usually be readily found in large numbers in discharges of gonorrhœal origin, but a diplococcus of similar appearance is also apparently to be found not infrequently in vaginal discharge of non-gonococcal origin. If a distinction is to be made it is best to try to grow the organism in question on the ordinary forms of culture media, as, while the gonococcus will not grow on plain agar, it grows freely on blood agar. On the other hand, the other forms of diplococcus met with in the vagina usually grow freely on plain agar. It is also possible that the presence of the diplococcus inside the pus cell is characteristic of the gonococcus, but one must be a trained microscopist, who is continually examining such preparations, to be certain that what appears to be inside the cell is not really lying directly below or above it. Therefore, in cases in which a diagnosis is of serious importance, it should never be based on a mere clinical examination.—J. E. R. McDonagh, Pr. Nov. '10.

**Acid Thionin.**—Thionin 0.5%, Glacial Acetic Acid 5% in Distilled Water. Stain 3 minutes, wash in tap water. A very reliable stain,—shows phagocytosis well and the characteristic "kidney" shape of the Cocci. Best stain for general use when confirmed by 'Gram.'—Wyatt Wingrave

**Jenner's Stain, q.v.,** also gives excellent results.

A case should not be diagnosed as positive from the presence alone of extracellular diplococci, as the extracellular life of the gonococcus is short, and even in a Gram negative examination, one cannot be always sure as to whether they are gonococci or no. The intracellular life is peculiar to the gonococcus, as it increases in the cell, without any apparent detriment to that cell, instead of being eaten up by the cell, as is usual, in other words, it becomes a "saprophyte."—Pr. Apl. /09,534.

**Nissl's Stain.**—Methylene Blue, 'B. Patent,' 3.75, Soft Soap 1.75, Water 1,000. Stain thin smears (fixed in air) without heating, for 1 minute, wash, blot and examine.—L. i./08,63.

**Other Diplococci:**—*D. albicans amplius* Bumm, found in mucus in the healthy vagina; *D. albicans tardissimus* morph. identical with the *Gonococcus*; *D. Coryzæ*, *D. intracellularis Meningitidis* (v Cerebro-spinal Fever), *D. of orchitis* found in gonorrhœal pus during the first two days—pathogenic), *D. pneumoniae*, syn. *pneumococcus* of Fränkel, q.v., *D. pyogenes ureæ*, and *D. Catarrhalis*. vide *M. Catarrhalis*.

*N.B.*—*Pneumococcus* is the only Gram + Diplococcus. Capsule well marked in pus, but not in culture. Cocci, elongated or lanceolate, converts oxy- into methæmoglobin in the culture. Will not grow on Gelatin.



**Hog Cholera.**—*B. Suipestifer* (or *Bacillus Ærtryck*) was isolated from cases of hog cholera, although this may really be due to a filterable virus. It has been found in the intestine of normal pigs, and may originate meat poisoning, especially where pork is the substance at fault. It shows close resemblance to *b-para*-typhosus B. and to demonstrate it the method of absorption or complement fixation must be employed.—M. & R., 6th Edn.

**Bacillus Influenzæ**, Pfeiffer's *Bacillus*, described in 1889-91. A very small bacillus, non-motile. Does not stain by Gram's method, nor grow on ordinary media unless albumen be present. Grows best on blood agar, but dies out rapidly unless subcultured every few days; can also be grown on glycerin agar. Present in sputum in cases of influenza. Stained by methylene blue the bacilli are very numerous in masses, but never seen in chains. See also L. ii./10,1289.

The *bacillus* is thought to play an important part not only in acute exacerbations of middle-ear suppuration, but also in primary attacks, an association first demonstrated by Pfeiffer himself. Owing to its feeble staining reaction it is easily overlooked, but if specially stained it is readily seen in acute cases of aural diseases, especially those complicated by osteomyelitis.—Wingrave, M.P.C. Sept. 23/08,343.

Post-Influenzal arthritis. Pyæmia due to this organism.—L. ii./07,685.

A number of cases of broncho-pneumonia occurring in one family. The Influenza bacillus, the only organism found—in the lung of one of the children—the apparent cause of death in all.—L. ii./09,1661.

The pneumococcus occurs very frequently in conjunction with the influenza bacillus. A mixed flora in the secretions in these cases is characteristic. Influenza bacilli are commonly found in the throat in pertussis, measles, and pulmonary tuberculosis. Not found in any of 11 cases of acute articular rheumatism.—B.M.J.E. ii./08,81; *c.f.* Vol. I., p. 891 and 314.

The Influenza Bacillus is thought to be only one of a group, the members of which have similar, if not identical, morphological and cultural characteristics but different pathogenic properties. In epidemic influenza Pfeiffer's organism is rarely found in the blood except as an agonal phenomenon. Nevertheless, in certain cases of endocarditis and of septicæmia an organism identical in all respects with *B. influenza* can be isolated, and is in all probability the cause of the illness. Organisms hitherto described as *B. influenza* are not all identical with it, but like the Strepto, Staphylo and Coli-typhoid family, belong to a group, the various members of which possess very different pathogenic powers.—H. Thursfield, Q. Jl. Med., Oct. '10, p. 1.

Influenza—Relation of so-called influenza to bronchitis and tuberculosis. Difficulties in the bacteriological diagnosis of influenza. It is more easy when occurring in epidemics. The microbes that do appear to cause 'influenza' are the tubercle bacillus, the pneumococcus, M. Catarrhalis, Staphylococci and Streptococci. Dangers of rash diagnosis of influenza. In 112 cases out of 416 unselected cases of tuberculosis of the lungs, the onset of the disease coincided with an attack of 'influenza.'—A. J. Jex-Blake, L. /13,1790.

For further details, *vide* our Vol. I, p. 887.

**Johne's Disease** in cattle (previously thought to be due to coccidia) has been identified with Johne's Bacillus—which is distinct from Tubercle Bacillus. F. W. Twort has grown the organism on the special culture medium used by him for isolating Leprosy Bacillus, *q.v.* Injections in guinea-pigs, rabbits, etc., produced negative results. Vaccines for the diagnosis of Johne's disease in cattle as distinct from tuberculosis may possibly be made. Communication to Roy Soc of Medicine, Nov. 1, 1910; Na. Nov. 24/10,127.

**Kala Azar**, Dum Dum Fever—characterised by persistent fever of alternating and intermittent type—certainly caused by a minute organism, which has been shown to be a stage of a flagellated parasite.—Leishmann-Donovan bodies, intracellular, probably a trypanosome.—L. i./07,486. Its differentiation and epidemiology.—L. i./07,643.

**Leishman-Donovan bodies** belong to a group of parasites which used to be classed together as *Herpetomonidae*. They may be round, oval or pyriform, measuring 2 to 3.5 $\mu$  increasing to 4 or 7 $\mu$  in the flagellate form, by 1.5 to 2 $\mu$  with a granular cytoplasm containing two chromatic masses. The larger, more rounded, stains slightly, the smaller, rod-shaped stains

deeply. From the latter a linear structure runs to the acute end. A vacuole is often present. They are found in large numbers in the liver, spleen, bone, marrow, lymphatic glands and mucosa of the intestines, in the blood of the femoral portal or hepatic veins, more rarely in the circulating blood shortly before death.

The present state of our knowledge is, that they cause the disease kala-azar and are probably spread by insects, but the particular carriers are not known.—A. Castellani and A. J. Chalmers, *Manual of Tropical Medicine*, 2nd Edition, p. 348. See also *Kala Azar and Tropical Sore*, W. B. Leishman. —*Ql. Jl. Med.*, Oct. 1911, 109.

In addition to the irregular fever there is progressive enlargement of the spleen, progressive wasting, swelling of feet and legs, diarrhoea simulating dysentery, and enlargement of the liver. It is almost invariably fatal.—*I.M.G. Jan.* 10/1907.

Good results have been obtained by injecting 20 to 90 minims of a solution made of Quinine Sulphate 32 grains, Dilute Sulphuric Acid 1 drachm, Distilled Water 4 drachms. Five minims of 2% Cocaine Solution is first injected; the needle is left inserted, the syringe withdrawn from it, the solution drawn up into it and injected after a couple of minutes into exactly the same place where the cocaine solution was injected. A certain amount of painless effusion is caused. Injections have to be repeated just before the effusion from the first injection has disappeared.—*Pres. June*, 1911.

Its connection with the dog and the bug in Madras.—*L. ii./09*, 1495.

Curative value of *Leishmania Culture 'Vaccine'*.—*B.M.J. i./12*, 540.

Atoxyl used in a case with some improvement, but ultimately fatal ending.—*B.M.J. ii./09*, 1614.

*Leishmania Donovanii* and *L. Tropica*.—*B.M.J. i./12*, 717. Transmission by bugs *v.* also *B.M.J. i./12*, 567, and *L. i./12*, 743.

Can kala-azar be spread by mosquitoes? According to Franchini in Italy at least it appears probable that the Leishman parasites are transmitted by anopheles. Further experiments on animals required to substantiate. *L. ii./12*, 249.

Oriental Sore.—Differences between this and Kala-Azar.—*B.M.J. ii./09*, 647, 1333.

Ponos, a disease occurring in two Greek islands, is apparently the same as Kala-Azar. The finding of the Leishman-Donovan body in splenic or hepatic puncture remains wanting to establish the identity of the two.—*B.M.J. ii./09*, 782.

## Leprosy.

The presence of *B. leprae* (Hansen's Bacillus).—The specific organism of Leprosy in the mosquito (*Culex pungens*) and in the bed bug (*Cimex lectularia*) was shown.—*L. i./06*, 1347.

Bacteriology and pathological anatomy of leprosy. Possible association of leprosy with other diseases, *e.g.*, tuberculosis in the same individual at the same time.—*J.M.H. McLeod.*—*L. ii./09*, 515.

From three cases of nodular leprosy an acid-fast bacillus isolated which by subculture through successive generations gave a pure growth possessing "certain peculiar characteristics resembling morphologically the bacillus of leprosy." The culture medium consisted of 250 Cc. of distilled volatile alkali of rotten fish, 250 Cc. of weak "Lemco" broth without salt or peptone, and 50 Cc. of milk. "After three days inoculation the culture of acid-fast bacteria was subcultured on nutrient agar and broth (without salt or peptone); a feebly acid-fast bacillus developed. Its acid-fastness was increased by growing in milk, the degree varying according to the fatty nature of the medium. Agar plate cultures were made and these, three days after inoculation showed discrete colonies about the size of a pin's head, opaque, orange-red, raised in the centre, humped and moist to the naked eye. After 48 hours' growth its appearance is as in the nodules of a leper. The cultures when tested on guinea pigs, white rats and rabbits, gave negative results. A monkey, after repeated injections with culture developed clinical signs of the disease, and showed nodules in which were found typical leprosy bacilli, but attempts to obtain a pure culture from the lesions proved unsuccessful. Ten cases of leprosy were tested with Vaccines prepared from these cultures, "two have now recovered; two are so much improved that apparently the remnants of the disease are very slight, and the remaining six have all improved in a remarkable manner."—E. R. Rost, *I.M.S.*—*B.M.J. i./11*, 184.



Captain Williams has grown from cases of leprosy four types of organisms which are thought to be four phases of pleomorphic streptothrix,—an *acid-fast* and a *non-acid-fast bacillus* and an *acid-fast and non-acid-fast streptothrix*. It seems that the acid-fast streptothrix form can be converted into a non-acid-fast bacillus by change in the cultural environments. The four different types may be regarded as four different phases of the *same micro-organism*. He further describes a Vaccine prepared from cultures of the Acid-fast Streptothrix for which he claims immunising and possibly curative properties. — B.M.J. ii./II,184; L. ii./II,109; see also B.M.J. i./12,300,392; L. i./12,741.

Leprosy is possibly conveyed by the bed bug, but the 'fish hypothesis' is supported by Sir J. Hutchinson. The disease does not spread in the neighbourhood of leper establishments.—B.M.J. ii./II,463.

Some interesting experiments to determine mode of transmission of leprosy show that flies, mosquitoes and other insects may spread it but in particular *Acanthia lectularia* appears to constitute a very important agent in the spread. Acid-fast bacilli resembling *B. leprae* have been found in 30% of specimens up to 16 days after feeding on lepers.—T. Lindsay Sandes.—B.M.J. ii./II,469.

Bed bugs obtained from huts which had never been inhabited by lepers were caused to bite lepers near leprosy nodules on the face,—in every case they contained the bacilli. Experiments to determine how long they remain in the bug's body, etc., in progress.—E. C. Long.—B.M.J. ii./II,470

Love of the leper for fish diet generally in a state of decomposition.—B.M.J. i./II,1234.

Leprosy can under certain circumstances be transmitted to animals.—B.M.J. i./12,424.

A thorough disinfection of the nose is one of the first essentials in treatment. A solution of **Ammonium Persulphate** 3·7% and **Hydrochloric Acid** 1% in water has been used. Inhalation of the fumes of burning sulphur has also been employed.

A Parliamentary Paper (January, 1912) reports on **Nastin** (*vide* XIV. Edition) and **Benzoyl Chloride** in treatment of leprosy at the Mahaica Leper Asylum, British Guiana. Nastin has very little beneficial effect. Benzoyl Chloride in Petroleum Oil is extremely valuable as a nasal spray or paint to ulcerating surfaces—its regular use for such purposes is strongly advised. Further on Nastin.—L. i./13,335.

**Leprosy and Goats.**—Apparent connection between. Leprosy is held to be not transmitted direct from man to man. The goat is suspected to be the intermediary. As goats have gone out of 'cultivation' with the increase of cattle and sheep, leprosy has diminished. Two types of tuberculosis have been found in the goat, one identical with bovine and the other totally different, producing internal nodules resembling those found in lepers. Tuberculin prepared from infected goats would probably have remedial value for lepers.—B.M.J. i./13,253; P.J. i./13,308; *c.f.*, also Vol. I. p. 544 and Vol. II., p. 342.

In treatment early diagnosis and arrest are essential.

A cultural extract of the organism made on lines of Tuberculin oil has given good results at Charing Cross Hospital in early macular cases, but it is not of real advantage in advanced nodular cases.—H. Bayon, L. ii./13,1529.

**Bacillus Lepræ** has morphology similar to *B. tuberculosis*, but usually occurs more in clumps and are said to be tapered at the ends. Stain irregularly, and are more readily decolourised than *B. tuberculosis* by inorganic acids. Gram +.

**FURTHER NOTES ON ISOLATION AND CULTURE.**—Leprosy material from a typical leper was placed in 2% **Ericolin Solution** to kill contaminating micro-organisms and then inoculated on the following tubercle medium:—Egg 3 parts, 0·8% **Sodium Chloride** 1 part, ground **Tubercle Bacilli** 1% and **Glycerin** 5% or less, mixed, placed in tubes, sterilised and set in slopes. On this the *Lepra Bacillus* grew very slowly as a delicate colourless streak along the inoculated track and showed the typical morphological and staining

characters of the *Lepra Bacillus*; the *Bacillus* could be subcultured only on the Tubercle Medium.—F. W. Twort, P.R.S.M. Nov 1, 1910; B.M.J. ii./10, 1919; Na. Nov. 24/10, 127.

A general review of the drugs used in leprosy. Chaulmoogra Oil affects the disease favourably, but it is not a cure. "X" Rays useful, but they have their limitations. Clegg working independently at Manilla has succeeded in cultivating an acid-fast bacillus from the spleen and nodules on the ear of leper patients. He prepared a Vaccine, also a Glycerin Extract and Soap Solution. Treatment by these means was tried upon a number of lepers during a period of over 12 months, but in no case with any perceptible benefit. The Glycerin Extract had no action on the skin of leprosy or normal persons. A remedy for leprosy is still wanted.—L. i./II, 1523, *c.f.* F. W. Twort's work, above.

It is possible that the Hansen's bacillus is merely a harmless accompaniment of the real organism. It is possible to cultivate from cases of human leprosy a diphtheroid organism which acquires acid-fast properties on being injected into rats or mice.

Besides the culture of an acid-fast or other organism, complete animal experiments and extensive serological tests are necessary before a statement as to its relationship to the disease can be made. Mice or rats injected with a culture of acid-fast diphtheroid bacilli originally obtained from acid resisting diphtheroid organisms of human leprosy, are capable of giving a culture of an acid-fast rod-shaped bacterium which when injected into other rats gives rise to what appears analogous to genuine spontaneous rat leprosy. The most favourable medium for growth appears to be either Placental-Extract-Agar or Horse Serum-Nutrose-Agar with the addition of 2% ground-up *Smegma Bacilli*. The author confirms *Kedrowsky's* work on the variable morphology and staining properties of the *Lepra Bacillus*. Agglutination, precipitation, complement-deviation and percutaneous tests can be used to prove the relationship of acid-fast or other germs cultured from cases of leprosy. Rat and human leprosy appear to be identical diseases. It is therefore possible that the germ of both can be transmitted from one to the other given an appropriate intermediary.—Bayon, B.M.J. ii./II 1269; L. ii./II 460.

### **Recent Papers on Leprosy.**

The organisms isolated from the lesion of human leprosy.—C. Duval, B.M.J. ii./12, 1189. Problem of leprosy, M. E. Marchoux, *ibid.* 1191. Study of various cultures of *B. Lepræ*.—H. Bayon, *ibid.* 1191. See also *Annus Medicus* L. ii./12, 1791.

Bed bugs and leprosy. Preliminary note. The results of examination of bed bugs fed experimentally on nodules of lepers at the Royal Southern Hospital, Liverpool, as also examination of bed bugs fed on lepers in Panama were entirely negative.—David Thomson, B.M.J. ii./13, 849.

### **Malaria** (*c.f.* also *Vol. I.*, p. 887).

To combat malaria in India and other places where it is prevalent it is necessary:—

(1) To improve the surface drainage and prevent the formation of puddles where the larvæ can breed, also to remove the vegetation surrounding such, and for the wealthy to do away with or cleanse weekly the ornamental waters in their gardens. Smoke is a wonderful protector against malaria, and it is customary in certain parts to burn dung and such-like during the night in huts and stables.

It has been found that formaldehyde evaporised from tablets of Paraform is of little avail to kill mosquitoes in a room—probably Sulphur Dioxide would do more, or nitrous fumes made by action of Nitric Acid on copper, or even a little Nitric or Sulphuric Acid strongly heated in the sealed room—destructible fabrics being removed—would be more successful.

(2) Protection by means of wire gauze.

(3) Distribution of quinine, *vide* also p. 645 (quinine is distributed gratis by the country pharmacists to the poor in Italy).

The young *Culex* larvæ have been proved to survive desiccation for several months. Certain of the adult culices (*Culex impellans*) appear to prefer to attack birds rather than human beings, the avian blood being recognisable on dissection of the insect.

It is a remarkable fact that so far inoculation experiments on all animals excepting man have proved unsuccessful, and in the case of man the inoculation should be intravenous. Experiments have found, however, that malaria can be produced by allowing infected mosquitoes to bite healthy individuals.



The Anopheles larvæ are easily found in the winter in sun-exposed, grass-surrounded pools in the infected districts in India.

The method of killing the larvæ, and indeed, all other water insects, beetles &c., is to pour common kerosene on to the surface with the aid of a sprinkling water-can. This forms a scum, which prevents the larvæ from breathing the atmospheric air. They die and sink to the bottom, or are washed up on to the banks in countless numbers. Thirty pounds of oil will cover at least 2,000 square yards of water; the dose of paraffin should be repeated about 20 times during the year.

Rice cultivation with the necessary stagnant water is no small source of increase of malarial disease.

Major Ronald Ross has stated that in spite of all ascertained facts *re* malaria, in spite of the parasite having been cultivated in the insects over and over again, in spite of the infection having been produced experimentally in men and birds by their bites, &c., &c., not one in 20, even in malarial districts, believes the theory. Extirpation of mosquitoes in tropical countries needs Government action.

There remain a few difficulties to settle in the mosquito theory, *e.g.*, how it comes about that the proportion of infected mosquitoes reported in certain districts was only 1·6%, whereas the percentage of natives suffering from the disease was high as 48·5%. Again, large tracts of land in Erythrea have no human inhabitants. It is possible to contract malaria by sleeping there in the open for a single night; how does the insect causing that infection (which it undoubtedly does) become infected?

Ross on Malaria in Bœotia, Greece;—

Adult natives of a malarious district become comparatively immune. It is necessary to examine the children. Out of the selected children to the number of 292, in five different parts, 97 showed evidence of malaria, *i.e.*, one-third. The Anophelines—the larvæ of *myzomia maculipennis*—were found in the pools. These small surface pools have to be removed to rid the land of the scourge.—L. ii./06,1386.

Occurrence of malaria without the agency of Anophelines. Outbreak in Picard Island in the Seychelles, Anophelines were searched for, but were not found. Up to the present no other mosquito has been shown to be efficient host for the malaria parasite. Possibly *Culex* or *Stegomyia*, which were present, may in certain circumstances act as carriers, but on the other hand the Anophelines may have been borne by ship.—L. ii./09,237. B.M.J. ii./09,99.

Attempts to exterminate malaria-bearing mosquitoes at Mian Mir in India failed.—L. ii./09,428.

Malarial fevers ordinarily claim one million deaths annually.—L. ii./09,1231, 1470.

The decadence of Greece due to malaria and its consequences.—B.M.J. i./09,1349.

Recurrence of malaria after 7 years, application of bacteriological methods concerning immunity to protozoa useless.—B.M.J. ii./09,769.

J. Cantlie relates that Quinine, Calomel and Salicylate had no effect on malarial fever and neuritis, whilst a change of air and exercise effected cure. Advice as to climate for malarial sufferers.—B.M.J. ii./09,769.

Malaria, latent, indicated by Urobilin.—B.M.J. ii./08,1357.

Prof. Ronald Ross advocates systematic *enumeration of the number of organisms* present in men or animals infected with given parasites. The mere detection of the parasites is not enough,—by counting before and after a dose of a drug, more exact criterion of its effects could be obtained. 'Counting' in 33 cases of malaria,—one of *P. Malaria*, eight of *P. Vivax*, and 24 of *P. Falciparum* showed that the numbers of asexual forms diminished after the febrile period until about the middle of the apyrexial interval, after which they gradually increase until they are numerous enough to cause a relapse. Quinine is not immediately lethal on all the parasites. Methylene Blue and Soamin have little effect on the asexual forms, though the former is thought to affect crescent forms, which remain very refractory to quinine.—'Enumeration' under Quinine is wanted.—L. i./11,585.

For information on the subject—the number of parasites that may be introduced by the mosquito—the reader is referred to “**MALARIA PREVENTION**” by Major Ronald Ross:—

He advocates a study of the numbers and local distribution of the particular anopheline mosquitoes which are found to transmit malaria in a given locality, an accurate measure of the amount of malaria present in a particular population under Quinine and other preventive measures, the estimation of the number who show signs of present or recent infection by enlargement of the spleen, the constantly-sick-rate, the death-rate, etc. He concludes that the most generally useful of these is the *spleen-rate*, since an actual microscopical examination of the blood demands too great labour. In this connection it is stated, reasoning shows that in a quarter of an hour a careful microscopical examination of a sample of blood for parasites will only have searched 1/50th of a C.mm. *Since this volume is only about 1/150,000,000 of the blood in a man's body, it follows that there is a considerable chance that not a single parasite might be detected, although the individual might have 150 million of them in his circulation at the time!*—From a review.—Na. Dec. 29, 1910.

**Anti-mosquito measures in India.** Second meeting of the **General Malaria Committee.** Investigation of the *Leishmania* type of diseases allied to malaria, viz., *L. donovani*, the parasite of Kala-azar, *L. tropica*, the parasite of oriental sore, and *L. Infantum*, the parasite of infantile splenomegaly in N. Africa essential. Educational anti-malaria measures necessary. Quinine prophylaxis should go hand in hand with general sanitation and destruction of *Anopheles* breeding grounds. *Stegomyia* may prove an even greater danger in the immediate future in India in view of the importation of yellow fever.—B.M.J. i./12,23.

Fairs are prolific sources of malaria in India. Result of investigation of a village away from *Anopheles* breeding grounds where constant infection occurred.—L. ii./12,1387.

**Malarial Parasites.**—The mosquito theory of this disease was established by Ronald Ross, the winner of the 1902 Nobel prize; after Manson, Golgi, and others had paved the way to a great extent. The *Culex pipiens* or common mosquito it is thought does not convey malaria. It is the Spot-wing or *Anopheles maculipennis*, also belonging to the *Culicidæ*, which carries infection.

(No fewer than 82 genera of the *Culicidæ* are now described.—Allbutt's System of Medicine.)

The female *Culex* has the palp much shorter than the proboscis, whereas that of the female *Anopheles* is almost the same length as the proboscis. The body of the *Anopheles* stands at an angle with the surface on which it is resting, whereas the body of *Culex* is almost always parallel with it.

The female is frequently found with its body ‘blown out’ with blood which it has imbibed. This *Anopheles* is common throughout the world. The males are harmless as far as blood sucking is concerned. The Midges (*Chironomidæ*) which dance and ‘swarm’ in the evenings are quite harmless. Important differences in venation and hairs on the wings enable one to distinguish between *Culicidæ* and *Chironomidæ* with certainty. The *Anopheles* goes through the stages of ovum, larva, and pupa; the mosquito lives in the water.

Laveran, the discoverer of the parasite of malaria which is known as *Hæmaphys*, previously called *Plasmodium* or *Hæmatozoon malaricæ*, divided it into the following phases:—1, spherical bodies; 2, flagellated; 3, crescents; 4, rosette forms.

(Some observers, contrary to Laveran, have been of opinion that the different types of malaria are due to different species of the organism.)



The whole life history of the Plasmodium will be found illustrated by some excellent models at the Natural History Museum, South Kensington, London. Briefly in the tertian form the spore, which is freely swimming in the blood plasma enters the corpuscle. It develops amœboid movement and then shows pigmentation owing to changes in the hæmoglobin. A nucleus is developed. The rosette form is the next change owing to division of the Karyosomes. On breaking up, the spores are liberated into the blood, the spore emission being synchronous with the attacks of renewed fever.

There are two distinct cycles of existence, one in the human being (asexual) and the other (sexual) in the mosquito.

Furthermore, there are at least three distinct species of the parasite infecting man :—

(i) **Quartan**.—This completes its cycle in about 72 hours—there is pyrexia every third day ; double or triple infection may, however, occur. In the case of this species only the smaller forms show movement (which is not pronounced as in the **Tertian**). The pigment granules are coarse and almost black in colour. The rosette contains 6 to 12 spores, and the red corpuscles retain their colour and size.

(ii) **Mild or Benign Tertian**.—The parasite matures in 48 hours, though by double infection a quotidian form may be produced. The outline of the amœbulæ is less refractive than in the Quartan. Movement is much more active. **Schüffner's Dots** may be observed on staining, in the infected corpuscles. The rosette is somewhat larger than in the Quartan, and gives 15 to 20 somewhat oval spores.

In addition there is the **Æstivo-Autumnal** or '**Malignant**' or **Tropical Malaria** parasite. The cycle of change is difficult to follow, it probably occupies 48 hours ; the young parasites are very small but active, which, however, change into the resting 'ring-forms.' Pigment granules are small and few in number. The fully developed sporocyte occupies less than  $\frac{1}{2}$  the red corpuscle, and yields usually 6 to 12 spores—irregular and minute. Sporulation occurs internally, hence sporocytes not seen as with (i) and (ii) in the peripheral blood. "Crescent" forms are seen, but they do not appear in the blood until several days after the onset of the fever. They are extremely resistant to quinine. These crescents are the male and female gametes ; it is possible to observe the male changing into spherical bodies which will flagellate whilst the others will not. The gametes are not crescent-shaped in the other forms of malaria.

For quinine treatment, *v. Vol. I.* 645, 651, 887 and 888.

#### *Staining Methods.*

Films of blood smeared evenly with a very small quantity *s.a.*, dried in the air, not by aid of a flame, and fixed by immersing in alcohol and ether, equal parts, 10 minutes, may be stained with aqueous methylene blue and eosin, or with methylene blue alone, 5 minutes, or with a Hæmatoxylin Stain, or by **Leishman's Stain** (*q.v.*). With Leishman's Stain fixing is not necessary. **Muir** says the structure of the parasites is well brought out by the following—Soak film in Saturated Corrosive Sublimate Solution a few seconds. Wash well, stain with hæmalum 10 minutes, wash, stain again for about the same time with aqueous methylene blue. Wash in water, dehydrate, clear in Xylol and mount in balsam. The chromatin of the parasites is violet blue, and the protoplasm pure blue. The Leishman method is, however, principally in use. Consult *Allbutt's System of Medicine*, or *M. & R.*

#### **Malaria—rapid method of Diagnosis.**

Thick Films are examined—the thicker part first before even dry—the diffuse and fine dots of tertian, the compact and coarse dots of quartan, and the peculiar arrangement of the pigments in the crescent in tropical malaria are very characteristic—not to mention pigmented leucocytes, be sure the pigment is on the same level as the red corpuscles and disappears totally on focussing up and down.—*J. Cropper, B.M.J. i./12,890.*

Two mosquitoes *Pyretophorus costalis* and *Myzomyia funesta* responsible for the spread of, in Madagascar.—*B.M.J. ii./06,1056.*

Panama, the most difficult place to rid of the scourge, nevertheless *Anopheles* and *Stegomyia* practically abolished from the Canal zone.—*B.M.J. i./07,401.*

Unsolved problems and troublesome symptoms in malaria.—*B.M.J. i./07,687.*

A table of tropical diseases, showing their germ causes and intermediaries. A lecture dealing with the subject, tropical temperature is necessary for the growth of the intermediary.—*Sir P. Manson, L. ii./08,991.*

Steps to be taken in Malarial districts, treatment of watercourses, houses &c.—B.M.J. ii./07,1044 *et seq.*

### **Cultivation.**

The malaria parasite is stated to have been cultivated. The medium employed being Locke's fluid, omitting Calcium Chloride but adding human serum or ascitic fluid, the addition of Dextrose being generally advisable. The cultures were carried on for four generations. Leucocytes had to be excluded from the culture medium as they phagocytosed the parasites at the period of segmentation.—Review of Tropical Diseases.—Pr., Aug., '13, 218.

**Locke's Artificial Serum.**—Sodium Chloride 1 Gm., Potassium Chloride 0.01 Gm., Calcium Chloride 0.02 Gm., Water 100 Cc.—Merck's Reagenzien Verzeichniss, 1913.

Another formula is given with Sodium Bicarbonate 0.02 Gm., and Glucose 0.1 Gm. in addition—the water being first slightly acidified.

**Schlesinger's Solution** (Zinc Acetate 1, Alcohol 10).—As test for malaria depends on the fact that Urobilin always present in the urine is increased in amount in this disease. Take 1/3rd test tubeful of urine, add equal volume of Schlesinger's Solution and then a few drops of a weak dilution of Iodine Tincture. Absence of fluorescence is strong evidence against acute malarial fever.—L. i./13, 1803.

**Peritonitis, Bacteriology of.** Frequent presence of a *Staphylococcus albus*.—L. i./06, 1250.

### **Bacillus Pestis (Bacillus of Bubonic Plague).**

*For Symptoms, Prophylactic and Curative treatment vide Vol. I., p. 889.*

**Bacteriology.**—Specimens from the buboes show coccus-like forms. They were first found by Kitasato in 1894.—L. ii./98, 428.

**Culture.**—Yersin first described the cultural properties.

**Morphology.**—Short fat bacillus. On staining with weak aniline dye shows marked polar staining. Spores have not been demonstrated. Non-motile. Does not retain the stain when treated by Gram's method; grows well on usual media (? potato) both at room and body temperature. Does not liquefy gelatin. Occurs in chains when grown in fluid media. Forms typical stalactite growths in bouillon and in presence of butter fat, but must be kept undisturbed (Haffkine). Man is inoculated through the broken skin.

Further work on the Bacillus.—B.M.J. ii./05, 735.—B.M.J. i./07, 691.

The bacillus produces alkali in its growth, which ultimately causes stoppage of its growth (in broth). The amount of alkali produced is equivalent to 1.5 to 2.5% normal Sodium Hydroxide (solution), and this amount reached in 6 to 8 weeks, causes arrest of the growth, but not death of the bacillus.—L. ii./08, 1620.

In smears made at an early stage of the disease from the buboes, expectoration or blood respectively in the three varieties of plague, the bacillus is present in enormous numbers, and the films show "polar staining," the centre being hardly stained at all; this is characteristic. In older lesions peculiar, large, rounded or ovoid "involution" forms of the bacillus are met with. The organism is readily destroyed by heat (60° to 65° C. for ten to fifteen minutes), and by disinfectants. The plague bacillus is pathogenic for a number of animals, in addition to man—the rat, mouse, guinea-pig, rabbit, hare, ferret, cat, monkey, etc. In the United States the ground squirrels are attacked.—R. T. Hewlett, Na. Dec. 22, 1910, p. 237.

### **Epidemiology and Characters of Plague.**—

**Rat-flea Plague theory.** Clinical experience shows that plague has no preferential temperature, though the Third Report of the Plague Commission sought to establish a "climatic plague temperature" of 85° to 50° F. Calcutta is remarkably free from human fleas; dog fleas are prevalent on the other hand, and rat fleas are seldom or never found. Rat fleas do not bite men, on the contrary they have a strong distaste for the skin of man. Evidence of equally conclusive nature in the opposite direction by a Member of the Commission. Sir Havelock Charles states that it is a fact that there is always an association between rats and plague in India.—B.M.J. ii./08, 1357.

A remarkable feature which has characterised plague from the earliest times is the alternation of periods of widespread prevalence, "pandemics" with periods of quiescence and complete intermission. There have always



been localities in which plague has been 'endemic,' i.e., continuously prevalent, for example, on the Persian Gulf, in Asia Minor, and in Yunnan, a province of China bordering on Burmah and Tibet. Infection from man to man is almost negligible, the rat fleas being the intermediaries between the rat and man, and mechanically conveying the infection—the plague bacilli—from rat to rat, and from rat to man (*vide* an article by Dr. Petrie in "Nature," Nov. 3, 1910, p. 15), the destruction of rats is therefore essential. The disease exhibits a marked seasonal prevalence. In Poona plague is epidemic only from July to February; August, September, and October being the months of maximum prevalence. This period corresponds closely with the extent of flea prevalence on the rats. An epidemic terminates naturally, owing to a combination of adverse factors, e.g., decrease in the number of fleas, decrease in the number of rats, and an increase in the proportion of immune to susceptible rats. In some instances plague cases may be completely absent between the seasons of prevalence, but by what means the infection is kept alive in the intervals has not yet been determined. Rats are occasionally met with suffering from what has been regarded as chronic plague, but the latest investigations of the Indian Plague Committee indicate that the condition is one of recovery from plague infection, and the condition is stated to possess no significance in the seasonal recurrence of the disease among the rats. The recent outbreak of plague in Suffolk, though in itself insignificant is disquieting owing to the fact that plague-infected animals—rats, rabbits, hares, a ferret and a cat—have been met with in five districts in Suffolk, in one district in Essex, and in the London Docks, indicating a somewhat wide distribution of infected localities."—R. T. Hewlett, Na., Dec. 22 1910, p. 237.

The character of the disease seems to change from bubonic in summer pulmonary plague in the cold season.—L. ii./II, 1311.

#### Notes on the *Memorandum on Plague* of the Local Government Board.

The "ambulant" form of plague is referred to, and it is stated that persons with this type of the disease may spread the infection. Spread of infection by such persons would seem, however, to be very doubtful by direct personal contagion at least, and it is equally doubtful whether effective carriers of the disease in the sense of typhoid carriers exist. The evidence for the existence of such carriers is not satisfactory, and although the possibility of the occurrence of "pneumonic" carriers must be considered, the rarity of this type, at least in India, and its extreme fatality, considerably limit its importance from this point of view.

There is little or no liability to infection from contaminated food. This is justified by the accurate observations on the pathology of human plague made some years ago in Bombay by the Austrian Plague Commission, and by the results of experiments on susceptible animals. The memorandum deals fully with rat destruction. Kitasato has reported that in five years 4,800,000 rats were killed in Tokio alone at a considerable financial outlay, but that at the end of this time no appreciable decrease in the rat population could be detected. Kitasato attributed this to the circumstance that the rate of destruction, vigorous as it was, did not keep pace with the natural increase in the rat population. Recent experience in India appears to point in the same direction. It is beyond question, however, that so far as plague prevention is concerned, a great deal can be done in this country by diminishing or, preferably, abolishing rat infestation in human habitations and in their immediate neighbourhood.—G. F. Petrie, Na. Nov. 19, '10, 81.

The chance of human infection is determined by the number of hungry infected rat fleas, provided they will feed on man, and their

accessibility to man. It is pointed out that by various reasons there is not so great an 'accessibility' amongst Europeans as in India. The importance of finding plague infected rats at Wapping in June, 1911, would be greatly exaggerated if it were measured by Indian experience. This is higher up the river than places where plague-infected rats had been previously found.—B.M.J. i./11,1476.

The **Plague in China** and the far East in the winter of 1910 and early spring of 1911, was of the *pneumonic type*—the more severe form—a very large proportion of the natives and Europeans attacked died. Up to April, 1911, the outbreak claimed 46,000 victims. The first outbreak in the winter of 1910 was among hunters of the rodent *Arctomys bobac*, known in English as the marmot, in Russia as the tarabagan, and in Chinese as the hanta,—an animal susceptible to epizootic plague infection. It was spread by these men returning home. The extreme cold induced an indoor existence, so parties of coolies travelling through the country slept under conditions of constant intimate contact,—there is little evidence of infection having been contracted in the open air. Those towns that had adopted preventive measures before they became badly infected practically escaped. Isolation of patients and their contacts, and disinfection, when efficiently carried out, have invariably been followed by diminution of the death-rate. Amongst the rats examined no instance of plague infection was found.—International Plague Conference, L. i./11,1117,1118,1152,1162. See also L. i./12,688.

The proportion of pneumonic cases in this epidemic caused some alarm. Though latest experimental evidence indicates that bubonic plague can only be caused by infected fleas, yet the writer has seen the transmission from the pneumonic to the bubonic without rats or fleas. The happiest thing to occur regarding the outbreak would have been for this pneumonic outbreak to become bubonic,—combined with the enforcing of sanitation in the infected area so as to limit the spread of the epidemic.—Pr. May 11, p. 623.

### The transmission of Plague.

Plague is apparently the only bacterial disease transmitted to man through the medium of an insect. The rat flea combines the functions of culture tube and an inoculating needle with respect to spread of the epizootic, the blood imbibed by the flea being the culture medium. In a plague epidemic there are three conceivable infective agents:—the infected rat, the infected rat-flea and the infected human being (or human carriers). It is pointed out that if infected fleas were fed on rats immune to plague the infectivity of such fleas was much diminished. Immune opsonins in the imbibed blood favour the phagocytosis of the bacillus in the flea's stomach. The rat with acute septicæmic plague would seem to be the ultimate reservoir of the plague bacillus.—B.M.J. ii./10,1505.

Cats as plague preventers in India. They should come first in preventive measures.—B.M.J. ii. 10/305.

PLAGUE, SPREAD OF, B.M.A. DISCUSSION.—A history of Plague investigation starting with the discovery of the bacillus in 1894 by Kitasato and Yersin. Rats and the spread of, and true relation between epizootic and epidemic. Transference from rats to man. Chance of survival of the bacillus if deposited on soils and floors, viability of the bacillus in soils, food-stuffs, etc., alimentary infection, feeding experiments, transmission by fleas, experiments in flea-excluding houses, etc. Seasonal prevalence, the rat-flea hypothesis. The coincidence of the epidemic season with the period of greatest



flea prevalence seems to point to the position occupied by fleas as carriers. Rat fleas readily feed on man.—C. J. Martin. Opening paper,—B.M.J. ii.11/1249. *et seq.* This paper is a comprehensive resumé with a lengthy bibliography of facts established by the research of the Indian Plague Commission.

Flea infected clothes in India are spread on sand in the direct sunlight, in 45 minutes all are killed.—B.M.J. i/11, 1293; P.J. i/11 740.

#### PLAGUE AND ENGLISH LIFE.

The effect of plague in the past upon English national life has been very deep. Every English hedgerow is a reminder of plague. The hedgerows mark the change in land tenure which followed the Black Death. The pestilence produced a scarcity of labour which gave the final blow to villeinage and serfdom, and when farming in common ceased it became necessary to define the fields. From that period dates the emancipation of the English labouring classes. Plague helped to kill the textile industries of the Eastern Counties and laid the foundations of the modern prosperity of Lancashire and Yorkshire. It was largely responsible for the decline of the power and wealth of the monasteries, and thus brought nearer the Reformation. It facilitated the growth of English literature. Up to the time of the Black Death, French was the principal language of the schools and of the wealthy. So many teachers died in the epidemic that a new race of educationists arose who insisted on giving instruction in the English tongue, and the way was hereby paved for "Piers the Ploughman" and Chaucer. Europeans are no more exempt from plague than Asiatics. Their only protection is that their mode of life does not bring them into close contact with rats, or with the rat fleas.

He concludes by drawing attention to the danger to England of the few cases and the finding of plague rats in East Anglia, *c.f.*, *antea.*, also the warning of R. T. Hewlett, 'Nature,' Dec. 22, 1910, as to the danger to commerce in event of scattered outbreaks,—the Port of London would be in quarantine. The home and foreign trade of the Port now *amounts to nearly one million pounds per day.*—"Asiaticus," in the "Daily Mail," Feb. 15, 1911.

The only *true infectious cases are the pneumonic type*, and in these infection can readily be avoided by skilled nursing. The rat-fleas constitute the danger more than the rats. The fleas in question are not the ordinary kind,—they do not as a rule bite human beings.—B.M.J. ii./10, 1454. This is negated by the abstract.—B.M.J. i/11, 1476. *antea.*

Haffkine's Preventive Treatment which has saved many thousand lives is fully described in a pamphlet issued by the Research Defence Society.—B.M.J. ii./10 1471.

A small percentage of pneumonic cases in an outbreak is by no means a law of the disease.—B.M.J. ii./10, 1658.

Cow Dung as a Preventive.—This, it appears, is largely used in the huts in India—being spread on the floors liquid is allowed to dry—it is probably a source of great danger from tubercle, etc.—L. i./12, 700.

Opsonic Index in Plague Vaccination. An experimental investigation showing *inter alia* that the substance producing the rise in Opsonic Index in immune pest serum is the nucleo-protein contained in the bodies of the bacilli. The washed bacillary bodies do not cause any great increase in the Opsonic Index.—B.M.J. ii./12, 1098.

On the length of life of the rat-flea apart from its host.—B.M.J. ii./12, 926

A case of plague on a grain ship in the Tyne. Post mortem examination gave typical *B. Pestis*.—W. J. Tulloch, L. ii./13, 1318.

The Tarbagan (Mongolian Marmot) and plague. Exhaustive investigation into its possible cause of spread of plague. Not nearly so important as the rat—in this respect almost negligible.—L. ii./13, 529.

#### Pneumonia.

Fraenkel's *Pneumococcus*.—1. Prepare films from 'rusty' portion of sputum. 2. Stain by Gram's method and counterstain with eosin half to one minute. Stain other films by carbol-fuchsin. Overstain (five minutes). Slightly decolourise with weak acetic acid. (For capsule.)

To obtain a pure culture, the blood of a mouse dead from inoculation of sputum is sown on blood agar or Nasgar medium. Will not grow below 37° C.

**Recognition.**—Diplococcus (ends are often pointed—*Diplo lanceolatus*) sometimes occurs in short chains of four to ten cocci. Has a capsule, but this is absent in cultures. Gram's +.

Pneumococcic peritonitis in children, 15 cases reported.—L. i./o6,1591.

In an epidemic of influenza swabbings from the fauces frequently showed pneumococci in addition to Pfeiffer's Bacillus and Strepto and Staphylococci. In such cases (which invariably developed into pneumonia) it was considered that the influenza bacillus first weakened the resisting power of the lung and if pneumococci were present they invaded the weakened lung and produced pneumonia; where the pneumococci were associated with staphylo- and strepto- cocci a mixed infection and much more severe case resulted.—Pres., July, /o8,131. *Vide* also Vol. I., p. 890 and Vol. II., p. 303.

**CONJUNCTIVITIS, BACTERIOLOGY OF.**—In a school outbreak an organism morphologically identical with the pneumococcus but differing in fermentative activity and its non-pathogenicity to animals, usually highly susceptible.—L. ii./11,1418.

In cataract cases (at Prague) examination for pneumo and streptococci by growth in **Elschnigs' Culture Medium**, *vide* Culture media, is made and if found operation postponed with hourly applications of 1 in 5,000 Mercury Oxycyanide Solution until the organisms have disappeared. Simultaneously an Agar culture is made for diagnosing variety of Staphylococci if present.—E. W. Thomson, Glas. Med. Jl., Feb., 1913.

**Growth of the pneumococcus. Sir A. E. Wright's Serum Glucose Broth.**

1% Peptone, 1% Lemco, 2½ to 5% of human serum and an amount of alkali fixed by neutralising to Phenolphthalein and then adding 6 Cc. of normal acid to each litre of medium. 1% Glucose was found a valuable addition—the broth so made gave copious growth of pneumococcus.—L. i./14,1.

**Friedländer's Pneumobacillus.**—Present in only small proportion of cases of pneumonia. Common in influenza. Gram —, but stains well by carbo fuchsin.

**Recognition.**—A bacillus varying considerably in length; usually short, with rounded ends. Has a capsule. Is easily cultivated on all ordinary media.

**Characters.**—Best examined by dark ground or parabolic illumination. Gram—Stain by Gram's method but do not wash with alcohol, and omit any counter-stain. Hot Acid-Fuchsin gives good results.

**Polyomyelitis** (inflammation of the gray matter of the spinal cord). The virus of polyomyelitis stands midway between the finest and coarsest examples of 'filterable viruses.' It is highly resistant to drying, light and chemical action. In dust, especially with protein matter, it survives weeks and months—in diffusive daylight indefinitely and it resists the action of Glycerin and Carbolic Acid in 0.5% solution for months.—S. Flexner, L. ii./12,1451,1790.

**Bacillus proteus vulgaris** occurs frequently (50% of examinations) in chronic aural discharges. Like the colon bacillus, it stains with difficulty unless previously treated with iodine or potassium permanganate. It is Gram —and about 3μ in length, but may grow into long leptothrichial threads. It is nearly always associated with fœtor, and has the reputation of being a powerful ptomaine producer.—M.P., Sept. 23,/o8.

**Relapsing Fever, Syn. Recurrent Fever**, is associated with the presence of **Spirochæta Obermeieri** in the blood. In cases of relapsing fever terminating fatally the blood is frequently found to be teeming with the organisms. The corpuscles with the ½ inch oil immersion lens frequently appear to have slender spiral filaments attached to them, causing a rippling movement of the blood which persists for several hours when examined in the fresh condition.

Relapsing fever, Transmission by Ticks.—B.M.J. i. 13,65.

Noguchi has cultivated four species of pathogenic spirochetes occurring in the blood (as distinct from those which invade tissues)—*Sp. Pallidum* (q.v.) and that of yaws). The pathogenic blood Spirochetes cultivated include *Sp. Obermeieri* which is the cause of relapsing fever in Europe and the spirochaete of the fowl. He also has grown (nonpathogenic) Saprophytic Spirochetes, e.g., *Treponema macrodentium*, *T. microdentium*, *T. mucosum*, *T.*



refringens and *T. calligyrum*—a new species standing morphologically between *T. pallidum* and *T. refringens*.—B.M.J. ii./13,1100.

*S. Hata* cultivated Spirochetes of Recurrent Fever in a medium containing Horse Serum and buff coagulum. The virulence of cultivated spirochaetæ is relatively weak. Sir Wm. Leishman showed evidence of granule shedding in spirochaetosis and the development of the spirochaeta from the granule.—Int. Cong. of Medicine, 1913, L. ii./13,569.

Infection in lice by the spirillum of recurrent fever is hereditary contrary to previous views. The spirilla occur in the lacunary cavity of the insect not in the mouth organs or digestive apparatus. Inoculation does not take place from bites but through wounds in the animals caused by scratching. The animals become infected by the nails with fluid from crushed lice.—Ann. Inst. Pasteur per P.J. ii./13,729.

Spirochetes often occur in suppuration of middle ear (Wyatt Wingrave, Roy. Soc. Med., 1908) also in mouth and nose. *Sp. Refringens*, *Sp. dentium*, *Sp. buccolis*, *Sp. foetida*, &c. They are generally associated with *B. fusiformis*. Variable in size and shape, strongly resemble *Sp. obermeieri*. Attended by striking foetor.—M.P., Sept. 23/08, p. 342.

See also Tick Fever, p. 335.

### Ringworm Fungi. Rapid Clinical Method of Search:—

- (1) Soak the hairs in Potash Solution 10 minutes.
- (2) Wash in water to free from alkali.
- (3) Mount in Glycerin or Glycerin Jelly.

For permanent stained sections:—

- (1) Soak the hairs in Potash Solution 10 minutes.
- (2) Stain with Anilin Gentian Violet (*q.v.*) for 1 hour.
- (3) Absorb excess of stain.
- (4) Treat with Gram's Iodine Solution 2 minutes, wash in water. Decolourise with acidified Anilin Oil (Anilin Oil 10, Nitric Acid 1) for 15 to 20 minutes. Treat with Anilin Oil 1 minute, clarify in Xylol, and mount in Balsam.

The organism of *Favus* is *Achorion Schönleini* those of *Tinea tonsurans* (RINGWORM OF THE SCALP) and *T. circinata* (RINGWORM OF THE BODY), i.e., non-hairy skin, are *Microsporon Audouini*, *Tricophyton Megalosporonectothrix*, and *endothrix* (according as the fungus lies outside or inside the hair), that of *Tinea (Pityriasis) versicolor* is *Microsporon Furfur*.

Ringworm of the Scalp is rare in the adult.

*Tinea Barbæ* or *Hyphogenic Sycosis* (Ringworm of the beard) is a common affection of the beard. The common grey coccus inhabiting the upper layers of the epidermis may cause an infection and cause pustulation, but the fungus can be distinguished from this coccigenic variety. Syphilis may also sometimes simulate ringworm of the beard. *Eczema Marginatum* is a name for ringworm attacking the groins and axillæ. *Onychomycosis* or ringworm attacking the nails only—not common, but very troublesome.—For a useful clinical lecture on the subject v. M.P. Sept. 5, 1906.

Cultivation of Ringworm Fungi is possible on all ordinary media, but the addition of Glucose or Maltose is most favourable.

Nail ringworm and a case infected by washing of stockings, also one caused by mouse bite.—L. ii./08,238.

270 Ringworm patches in school children treated by X-rays. With exception of 5 cases, all were due to *Macrosporon Audouini*, 3 were due to *Megalosporon endothrix*, and the other 2 to *Tricophyton ectothrix*.—B.M.J. ii./09,454.

Suggested study of the question as to whether pediculi capitis are not carriers of ringworm infection,—thought to be so.—B.M.J. ii./11,780.

### Scarlatina or Scarlet Fever.

The viruses of scarlet fever, typhus fever, foot and mouth disease, measles and poliomyelitis are all filterable.

The greater number of diseases known to be due to filterable viruses affect the domestic animals—pleuro-pneumonia of cattle, African horse sickness, cattle plague, etc.—L. ii./12,1451.

Dr. Vipond, of Montreal, succeeded in isolating a spore-bearing bacillus from the mingled colonies of various organisms in cultures obtained from the enlarged glands of a child who died of scarlet fever and subsequently from six other cases, sometimes in pure growth.

The organism is a long bacillus with rounded ends, feebly motile, and an

active spore former. It stains variably with Gram's method sometimes showing a beaded structure. It grows well and rapidly on ordinary media. Monkeys have been inoculated with broth cultures and have exhibited enlargement of the lymphatic glands within 48 hours and well marked red rash in five days. One of the five monkeys died and from the glands *Post mortem*, the bacillus was recovered in pure culture. Requires confirmation.—Pr. July, 1912, 70.

Opinions from the large majority of 27 isolation hospitals in Great Britain were to the effect that too much importance has been attached to the **desquamation** as a source of infection. Milne, of Barnardo's Homes, does not isolate fever cases in any way, relying entirely on swabbing the throat with 10% Carbolic Oil and rubbing the body all over with Eucalyptus Oil (*q.v.*, Vol. I.). The poison in 99% of cases enters by the throat, hence patient is not free from infection till the throat is quite healthy again.—C. H. Phillips, L. ii./12,522.

**p-Dimethylamidobenzaldehyde Test.**—2 Gm. of this substance triturated with 30 Gm. Concentrated Hydrochloric Acid and diluted with 70 Cc. of water. A few drops of this solution added to the urine will by the red colour produced at once on heating confirm a suspected case of scarlet fever. The test depends on urobilinogen which is present in true scarlet fever.—M., 1913.

**Streptococcus Conglomeratus Vaccine** is prepared, but has not been subjected to a very considerable trial.

In most cases, with or without albuminuria, *Streptococci* are voided by the urine in large quantities in this fever

Various Drugs, taken internally or used locally, may occasionally, especially where idiosyncrasy exists, produce scarlatina-form rashes, *e.g.*, Venice Turpentine applied.—B.M.J. i./13,712.

### **Serpent Venom. Anti-venene.**

In the preparation of this serum the venom is removed either from the living snake or after killing it. This venom is mostly desiccated over sulphuric acid *in vacuo* and a weighed quantity of this is dissolved in sterile water and injected into the horse. The increase in dose proceeds very gradually; the final dose appears to be about 0.6 Gm. of venom, equivalent to the entire yield of 20 average sized snakes. The serum is removed in the customary manner and standardised.

Calmette showed that the venom of all snakes is of a similar nature, and obtained his remedy by the inoculation of horses with the poison of the cobra di capello; his serum possesses a strength of 1 in 20,000; that is to say  $\frac{1}{10}$  Cc. subcutaneously injected into a hare of two kilos in weight suffices to protect it from snake poison which kills a similar hare in eight hours.

It is claimed that anti-venomous sera are specific even between the venoms of a species of the same genus. An account of the serum therapeutics of number of cases.—L. ii./04,1273. *Vide* also L. i./06,1231.

Calmette has described the hæmolysins of snake poison; in addition to these bodies snake poison contains neurotoxins, which act on the nervous system, and cytolytins dissolving other tissue elements.—Bull. de l'Inst. Pasteur 'T,' v.p. 193.

**Dose.**—Anti-venene is supplied in tubes of 10 Cc. This amount or as much as 40 Cc. should be injected. The serum should be as fresh as possible. (As much as 400 Cc. intravenously and 10 or 20 times that amount, if subcutaneously, for cobra poisoning.—L. ii. 04,1273.) The injection requires to be made at once, or within an hour in man; death seldom occurs from serpent poison under three hours.

The dose of venom injected by a healthy cobra is about ten times as much as was assumed by Calmette, therefore the dose required to neutralise the poison should be ten times as much as that recommended by Calmette and Lamb.—Ghosh.

A ligature must be bound above the bite if possible. The wound should be opened up and washed with Chromic Acid or Gold Chloride 1% solution.

### **Skin, Tropical Diseases of.**—MacLeod, B.M.J. ii./05,1266.

**PINTA**, a disease caused by a fungus, producing discolourations on uncovered parts of the skin.—B.M.J. ii./05,1270.

**PITYRIASIS VERSICOLOR**, due to fungus growth under the skin, common in the tropics.—B.M.J. ii./05,1271.



**PELLAGRA.**—One of the chief plagues in Italy. *Aspergillus fumigatus* and *flavescens* said to be the cause. Some say it is hereditary.—B.M.J. ii./05,1273.

Pellagra is found in Europe, Africa, Asia, America, and even in Oceania, and probably affects more or less seriously over a million people. It is a disease of long duration, characterised by a peculiar rash, not unlike a severe sunburn which appears on the face, round the neck, and on the back of the hands and feet. This eruption recurs each year at determinate seasons (spring and autumn); it appears suddenly under the influence of exposure to sunlight, stands out some days, then fades off gradually, and is followed by long persistent desquamation. Together with the eruption other symptoms appear. They are irregular fever, frequent fits of giddiness with a peculiar sensation of falling backwards or forwards, great debility, confusion of mind, copious salivation, insomnia, pyrosis, and diarrhoea. These symptoms abate during the summer months and disappear almost entirely in winter, especially in early cases. They return with the rash each spring. After a period of progressive aggravation, which may last three, five, or thirty years, the patient becomes greatly emaciated, partly paralysed, and entirely demented. A number of these unfortunate beings commit suicide, as a rule by drowning; the majority end their days in the lunatic asylums of their respective countries. The disease affects the agricultural classes almost exclusively; town people are everywhere absolutely immune.—C.D. Oct. 22, 1910. From the *Times*, Oct. 15, 1910.

**PELLAGRA FIELD COMMISSION.**—Eating of Maize either sound or deteriorated can no longer be considered the cause of pellagra. A parasitic infection possibly conveyed by some insect. Pellagra occurs in districts where the sand-fly *Simulium* exists.—L. W. Sambon, L. ii./10,1709. B.M.J. ii./11,613.

Treatment by direct transfusion of blood. The recoveries (58%) following transfusion in the grave type of cases compares most favourably with the recoveries (10-20%) in the same type of case in which other therapeutic measures are employed. A few days after the transfusion gradual increase in body weight and improvement in mental condition was noticed. Recovery was established in a period varying from one to four months. No advantage has been noticed in the employment of a donor who has recovered from pellagra as compared with the donor who has never had pellagra.—B.M.J. ii./11,1276; L. ii./11,526; see also Investigation of.—L. ii./10,1709; L. ii./11,556,1524. In Egyptian prisons they are now using maize bread.—L. ii./11,916.

Pellagra is not transmitted by contact or association of persons. Although in Europe only the rural inhabitants are affected, in America it occurs among urban residents and even the well-to-do are not immune. Of all drugs perhaps Arsenic has most value as a remedy—it is best given *per os* as Fowler's Solution increased to 20 or 30 minims three times a day. Intramuscular injections of Sodium Cacodylate, Sodium Arsanilate, and Arsacetin have given good results in early cases.—Charles R. Box, Pr. June, '13,940.

Pellagra in England.—An account of four cases with description of the histological changes in the nervous system, also a history of the disease. Sambon believes pellagra to be an insect borne infection probably conveyed by a species of *Simulium*, a biting insect which passes its larval and pupal stages in running water. The disease is common in Italy. It has been showed to be endemic to a limited extent at least in some of the eastern districts of Scotland north of the Forth.—C. R. Box and F. W. Mott, B.M.J. ii./13,1.

Pellagra in Great Britain.—B.M.J. (Leader) ii./12,1155, *vide* also L. W. Sambon, B.M.J. ii./13,119,297, also 570, 584, 1445 (Leader on Etiology), 1773. Blackbirds transmit?—L. ii./12,251.

**YAWS (*Frambæsia Tropica*)** Treatment.—Sodium Bicarbonate in 1 drachm doses, together with Copper Sulphate locally.—B.M.J. ii./05,1275. Potassium Iodide 10 to 20 grains for adults, 2 to 5 grains for children thrice daily. If anæmic, Ammonio-Citrate of Iron. Locally Mercuric Nitrate Ointment (1 in 3 Vaseline).—B.M.J. ii./07,868.

**FRAMBÆSIA** in Ceylon. Potassium Iodide in large doses best routine treatment; Atoxyl, Sodium Cacodylate, and Quinine Cacodylate also useful.—L. ii./07,1458. Characters of the *Spirochæta*.—B.M.J. ii./07,1511. See also 'Salvarsan.'

**DHOBIE ITCH.**—Severe prurigo of the thighs is due to various Fungi.

**TINEA CIRCINATA.**—The fungi of this are distinct from those of dhobie itch, though all belong to Trichophytons.—B.M.J. ii./05,1278.

**PARANGI.**—(Allied to syphilis?) Spirochetes found.—B.M.J. ii./05, 1280.

**Sleeping Sickness**, see **Trypanosomiasis**.

**Sprue and Hill Diarrhœa**.—Features are sore tongue, stomatitis, peculiar form of diarrhœa, due to varieties of bacteria. Milk diet recommended.—B.M.J. ii./05, 1281. Trilactine (*q.v.*) should prove of value.

**Sporotrichosis** (due to *Sporotrichon beurmanni*).—A case of, treated by liberal doses of Potassium Iodide—80 grains per diem. Locally Iodine in the form of Gram's Solution is useful. The Iodine appears to act indirectly by stimulating absorption. Patient was in addition suffering from a ringworm infection (*Tricophyton Rosaceum*) of the nails. Cultural characteristics and peculiar properties of the fungus suggest that it may be overlooked. In all granulomata which cannot be clearly attributed to the ordinary causes of such lesions the possibility of Sporotrichosis should be kept in view.—B.M.J. ii./11, 1.

Sporotrichosis of the eyes, a number of cases. Sporothrix isolated from the pus from broken down nodules. Large doses of Potassium Iodide followed by rapid improvement both of the iritis and general condition.—Oph., Mar, 1911.

Beurmann states that there are several Sporotrichoses according to nature of the numerous parasites cited. That due to *S. beurmanni* is the most frequently met with. It has been found in many localities (cited). Full description of the parasite, parasitology, etiology, pathogenesis and diagnosis.—B.M.J. ii./12, 290.

**Staphylococci** are easily recognised by their grouping. They are Gram+ and smaller than streptococci, but whether *S. Aureus*, *albus*, or *citreus* cultivation gives growths, *e.g.*, on a tube of Agar, of the colours in question. They are the most easily grown of all the pathogenic bacteria.—Wingrave on aural discharges, M.P., Sept. 23, '08, 343.

**Hepatic Abscess**.—A case in which the patient had coughed up gallons of pus, arrived in England from India weighing 5½ stones—a mere skeleton. Open air treatment and a vaccine prepared from his organism (a *Staphylococcus*) obtained from the sputum restored to health (weight 12½ stones). Dose commencing with 5 million and advancing to 100 million. Examination of the blood prior to making the Vaccine showed patient's resisting power to this particular organism was non-existent. Other cases due to *S. lanceolatus* and *Staphylococcus aureus*.—Hale White and Eyre.—L. i./09, 610, 1588. See also Emetine, Vol. I.

A case of recurrent attacks of fever with endocarditis disturbance (Streptococcic infection) every three or four weeks, had an index falling to about 0.5 or lower just before the attack. After 4 or 5 days 1.2 or over when the attack ceased,—falling again after a week or two. A special Vaccine when the index had dropped to its lowest, caused a rapid rise and complete abortion of the attack. The injections were repeated several times with good result. A recurrent case of this kind throws light on the problem of recurrent sore throat with the possible sequel of endocardial infection.—Pr./09, 650.

**Streptococci** (Gram +) in aural discharges of two types:—

(1) *S. longus* (*S. pyogenes vel erysipelatus*) in long chains, (2) *S. brevis* in short chains is held to be pathogenic (*S. longus vel S. Salivarius*) which is common in the mouth and throat is said to be non-pathogenic. Marmorek, however, holds that the length of chain is variable, and Widal has shown that the non-pathogenic forms from the mouth when cultivated with B. Coli become pathogenic.—Wingrave.—M.P., Sept. 23, '08, p. 343.

See also **Septicæmia**. Vaccine Chapter. Vol. I.

It is thought that the strains of *Streptococci* and *Staphylococci* are as numerous as the varieties of 'Rubus' and the distinction of the colors 'Aureus,' 'Citreus,' 'Albus,' etc., do not by any means represent their numbers.—B.M.J. ii./10, 1115.

**Neutral Red Egg Medium** for cultivation of Staphylococci, see **Culture Media**.

**Syphilis**.—**Spirochæta Pallida**. *Syn.* Treponema Pallidum

*Spirochæta Pallida* has been cultivated by Noguchi. Absolute anaerobiosis is necessary.



Serum water, to which a piece of sterile rabbit tissue (preferably kidney or testicle) has been added, is inoculated from the artificially infected testicular tissue of the rabbit (not from human lesions). The Serum (in test tubes) is rendered suitable for anærobic cultivation by a layer of Paraffin Oil poured upon its surface. After the first cultivation strict anærobiosis is not essential—the organism can be subcultured on to solid media such as gelatin or agar. The first growths are usually contaminated by other bacteria. Two methods are suggested for separating these from the Spirochætæ:—(1) To grow the Spirochetes through filters which retard the passage of other organisms, or (2) a method depending on the fact that in stab cultures the Spirochetes grow away from the line of puncture into the surrounding medium, while other bacteria fail to do so. Noguchi states that Spirochetes cultivated by these methods are pathogenic in so far that after inoculation into the rabbit's testicle they produce characteristic histological changes and are found growing freely in the infected tissue.—H. Noguchi.—Jl. A. M. A., July 8, 1911, per L. ii./11, 536. B.M.J.E. ii./11, 48.

Noguchi's discovery of the Spirilla in the cortex cerebri of general paralysis. —B.M.J. i./13, 464; ii./13, 44.

*T. pallidum* has been transmitted from the brain of general paralytics to the rabbit by prolonged course of injections. Symptoms similar to those of general paralysis in man have been produced and the blood gave a positive Wassermann reaction.—B.M.J. ii./13, 1100, *c.f.* also **Relapsing Fever**.

Alive, may well be seen by parabolic ord ark ground illumination, *vide infra*. Dead by mixing film with liquid Indian Ink.—*vide Burri's Ink, infra*. The use of Collargol is satisfactory.

**Demonstration:** As they chiefly infest the lymph stream, the spirilla may be obtained by "needling" base of ulcer or adjacent enlarged gland. Make film, fix in warm air, and stain 12 hours by Giemsa's Solution at 37° C.; obtained only with difficulty from surface of ulcer.

**Characters.**—Gram negative. Smaller than *Sp. foetida*: regular and symmetrical corkscrew spirals, shorter than *Sp. buccalis*, greater number of turns. *Vide infra* for differentiation from other *spirochetes*.

### Life Cycle of the Organism.

McDonagh regards the long incubation period of syphilis as due to the cycle of changes which the organism must undergo before it can give rise to symptoms, and puts forward in explanation that one dose of Salvarsan, though it kills every spirochete in a chancre, does not cure syphilis—the reason being that other forms of the parasite are present which are not killed by Salvarsan. The Spirochæta pallida is never seen to divide, though present in enormous numbers in syphilitic lesions; this fact suggested that it was the end formed—the male sexual cycle. McDonagh states:—The commencement of the cycle is with a sporozoite or infective granule which by its mobility reaches and enters a cell, usually a mono-nuclear leucocyte. The sporozoite in some cases increases in size inside the cell, in other cases it divides; where there is no division, the development goes on until spirochetes are formed—the male sexual cycle. In the case where there is division, one half runs the course of the male sexual cycle, whilst the other runs the course of the female sexual cycle, the latter at this stage seeming to leave the lymphocyte. The act of fertilisation was not seen; the result of fertilisation is the production of a zygote within which by subdivision sporozoites are formed and ultimately set free to start the sexual cycles again. McDonagh classes this organism with the sporozoa, and suggests that the parasite is a leucocytozoon, which should be called the leucocytozoon syphilis. The infection is probably conveyed by the sporozoite and not by the Spirochæta Pallida.—P.R.S.M., Nov., 1912; P.J. ii./12, 809. *See also* L. ii./12, 1011, 1178, 1650; Pr., Dec., 1912.

The syphilitic spore has been shown to differ chemically from all the other phases met with in the life cycle of the '*Leucocytozoon Syphilides*'.—B.M.J. ii./13, 1611.

Complicated life cycle of *T. Pallidum* not agreed to by D'Este Emery. It remains a spirochete throughout.—L. i./14, 222.

**Giemsa's Stain.**—Dissolve Azur II.-Eosin 3 Gm. and Azur II. 0.8 Gm. (previously well dried in exsiccator before weighing, and powdered as finely as possible) in 250 Gm. Glycerin without heat, add Methyl Alcohol 250 Gm. Shake well, allow to stand at room temperature 24 hours and filter. It is convenient to keep a little of the stain thus made in a drop-bottle and add from this 1 or 2 drops of the stain to every Cc. of water in the staining bath. Staining of films or 'smears,' previously fixed in alcohol 15 minutes is allowed

to proceed for 15 to 60 minutes (Giemsa) in a shallow dish (some workers favour much longer), wash in water, dry and mount. Over-stained preparations should be treated with water to remove excess. See also B.M.J. ii./06, 738 for a more concise way of making.

The material called Azur II.-Eosin is composed of Methylene Azur and Methylene Blue in equal parts and Eosin chemically combined in a manner not stated by Giemsa in his papers.

#### **Giemsa Stain in two Solutions—Alternative Process.**

Prepare a 1% aqueous Azur Solution and a 1% aqueous Eosin Solution. To 1 Cc. of the Eosin Solution add 10 Cc. Distilled Water, then add 1 Cc. of the Azur Solution. Stain ten minutes or longer.—B.M.J. ii./06, 738.

Long and diligent search necessary in looking for the *Spirochæta* stained by this method. Table of this and other *Spirochæta*.—B.M.J. i./09 455.

This stain imparts to the spirochete a distinctly reddish violet tinge, similar to that of the neighbouring leucocyte nuclei (the Romanowsky chromatin stain), whilst the bacteria come out blue.—B.M.J. i./05, 1263.

Giemsa's Stain sometimes succeeds in demonstrating gonococci where the more common stains have failed. It should, therefore, be included in the routine method (McKee's method, Oph. Record, Jan., 1912), S. Stephenson, Pr., Sept., '14, 378.

#### **Examination of Unstained Specimens.**

The old methods of examining the spirochæta in the hanging drop, and by staining with Giemsa's Stain have been completely superseded by the Dark-ground illumination, the Chinese ink and Collargol methods.

**Ultramicroscope.**—Employed for demonstrating in a rapid, easy and certain manner the presence of the living organism. Useful to examine a scraping when it is necessary to give an opinion on a doubtful primary or secondary syphilitic lesion. Syphilis cannot of course be excluded because the organism cannot be detected on one examination.

The Ultramicroscope is a paraboloidal immersion-condenser. The rays of light used are deflected so that they converge obliquely on the object examined, which appears as a bright refractive body on a dark background. In this way very transparent objects which are invisible by direct elimination are easily seen.

*Treponema Pallidum* seen thus is an extremely fine silvery spiral from 6-15  $\mu$  in length, with very regular or closely set spirals (about 7 to the diameter of a red blood corpuscle). The spirals vary from 10-26 in number. Extremities are pointed. If so focussed that only the summits of the spirals are illuminated the organism looks like a series of bright dots, not unlike a chain of Streptococci. It is feebly motile, its movements consisting of rotations round its long axis, backward and forward movements, and bending movements, which are the most marked. It preserves its spiral form during rest.

*Sp. buccalis*, *Sp. refringens*, *Sp. balanitidis* are much larger with wider and more open spirals. *Sp. retringens* has only 3 to 5 turns and is usually blunt at either or both ends. The only spirochætes very like the specific organism are (1). *Sp. dentium*, found in carious teeth, which is shorter (5 to 10  $\mu$ ) and coarser, 5 to 15 spirals, the wave length the same as *T. pallidum*, but depth of wave is considerably less; (2). *Sp. pertenuis* (yaws), Castellani; (3). *Sp. pseudo-pallida*, Loewenthal (ulcerated cancers). In the last two the spirals are not quite so deep or regular, and in the case of *Spirochæta pertenuis* the ends are often twisted into rings or loops.

*Treponema Pallidum* is found below the surface in the lymph only and should be sought at the margin of the lesion. It cannot be detected in the centre of an ulcerated or necrosed area where the saprophytic spirochetes may be seen in large numbers. The organism is found in the largest numbers in mucous plaques, is constantly present in varying numbers in primary untreated chancres, and is usually detected in the papular syphilide and in scrapings from a recently removed enlarged syphilitic lymphatic gland.

The margin of the chancre, papules, or mucous plaque should be gently scraped till blood just begins to exude. The surface is now dried with a swab of plain sterile gauze, and then a little blood or serum expressed by decompression or by bandage. A small drop of this is removed with a platinum needle and mixed with a drop of distilled water on a thin glass-slide. A thin cover-glass is now pressed down firmly, so that only a thin layer of fluid remains between the slide and cover-glass. A drop of immersion oil is



placed below the slide and on the cover-glass. The condenser must first be accurately centred. This can easily be done with a low objective (1 in. or  $\frac{3}{4}$  in.) by means of concentric rings scratched on the surface of the condenser.

Any artificial light can be used—electric (arc or Nernst), gas (incandescent), or even an oil lamp. Concentrate the light to the centre of the microscope mirror. After the slide has been placed in position so that there is a layer of oil between the ultra-microscope and the under surface of slide, and after the object is focussed, the ultra-microscope must be racked up or down and the mirror adjusted till bright illumination with dark back-ground is obtained.

General or local treatment has a marked effect on the number of treponemata found, and the organisms tend to disappear after a few weeks from the site of the primary inoculation, even without treatment.—H. W. Bayly, P.R.S.M. Clin Sectn. Nov. '09, p. 3.

Antiseptics must not have been previously applied to the sore.—B.M.J. ii./II, 686.

**Chinese Ink Method (Burri).** The method is known in Germany as *Tusche Verfahren*. Burri's work, 1909, on the subject is published by Gustav Fischer, Jena.

The method requires no special apparatus. A platinum loopful of secretion from a sore is placed on a slide and mixed with an equal quantity of Distilled Water and an emulsion of Chinese Ink. The whole is mixed and spread on the slide like a blood film, allowed to dry and examined with oil immersion lens. The ink produces a dark background and the objects stand out white. It is easy to differentiate the two forms of spirochetes.—McDonagh, P.R.S.M. Apl. 1910, p. 73, Pr. Nov. 1910.

**Collargol Solution** 1 in 20 (store in Amber bottle) preferable to Chinese Ink. One drop with one drop of the suspected secretion to be mixed together and allowed to dry on slide, and then spread with another slide to make a thin film. The preparation is examined with  $\frac{1}{12}$  inch oil immersion lens—the background is perfectly homogeneous.—L. W. Harrison, B.M.J. ii./12, 1547.

Or proceed as follows.—Make a thin film, fix by radiant heat. Pour the Collargol Solution over film, decant quickly and stand up to dry in air or incubator. Examine with  $\frac{1}{12}$ th inch immersion lens.—Wyatt Wingrave.

#### Comparative Value of Staining Methods—

*Sp. Refringens* under dark-ground illumination is seen to shoot rapidly backwards and forwards in a straight line and when not rotating so actively is often seen to squirm its way by corkscrew movements, pushing blood corpuscles, bacilli, etc., aside. The diagrams illustrating this paper show the marked difference between this organism and *Sp. Pallida*. Serum obtained by swabbing is preferable for examinations to scrapings. In staining with *Giemsa's Stain* (diluted 1 in 8) at least 12 hours is best. In the *Indian Ink* method at least twice the volume of Indian Ink to the drop of serum. Spirochaetes are more constantly present in condylomata and mucous patches and far less constantly present in papular secondary skin eruptions than in primary sores. *Dark Ground Illumination* is the best method of examination.—B.M.J. ii./II, 1283.

#### Gentian Violet staining of *Sp. Pallida*.—

The stain is prepared on the lines of Gram's Anilin-Violet for bacteria:—

Shake 3 Cc. Anilin Oil with 20 Cc. distilled water for 5 or 10 minutes and to the filtered liquid add half its volume of a concentrated alcoholic solution of Gentian Violet. Fix smears by holding over 1% Osmic Acid Solution for one to two minutes. Pour the Stain over the specimen and heat 20 to 30 seconds over a flame. Wash off with water, dry and examine with oil immersion lens. Spirochaetes appear reddish-blue against a rose-colored ground.—*Sp. Refringens* being stained more deeply.—Klausner, Berl. Klin. Woch. Jan. 23, 1911, per L. i./II 321.

**Lead Subacetate Method.**—Fix with Osmic Acid as above, wash in water and cover for 10 seconds with a solution consisting of Liquor Plumbi Subacetatis 1, Water to 100. Again wash and cover 10 seconds with a 10% Aqueous Sodium Sulphide Solution. Wash and repeat whole process twice. Apply Osmic Acid Solution 30 seconds, wash and dry. Spirochaetes, cell debris and bacteria appear black.—A. A. W. Ghoreyeb. Publications of Mass. Gen. Hosp. vol. III, No. 2, p. 367, Jl. A.M.A. May 7, 1910, per L. i./II, 321.

**Silver Method (Tribondeau).**—Use material from infiltrated tissues around chancre not from surface. Eliminate hæmoglobin, etc., as far as possible by washing (*v. infra*). The *fixative* used consists of Formalin 2 Gm. Acetic Acid (Pure) 1 Gm., Water 100 Cc. The *Mordant* is 5% Tannin in Water. The Silver Stain is Silver Nitrate 1 Gm., in Water 20 Cc. To 15 Cc. of this add Ammonia drop by drop until precipitate redissolves; then add the remaining 5 Cc. of Silver Nitrate Solution until the solution remains slightly opaque after shaking.

**Technique.**—Dry smear at 37° C. Fix by washing with fixative one minute and complete by a few drops of Absolute Alcohol, allowing same to dry on the inclined slide. Add the Mordant and warm over flame till just steaming for 30 seconds. Wash, pour off excess and without drying employ the Silver Stain over a flame for thirty seconds. Wash and dry. *Sp. Refringens* and *Balanitidis* are darker and distinguished by their morphological character.—B.M.J.E. i./13,16.

The method is very similar to Van Ermengem's process for flagella—one cannot be certain of getting results every time.—W. D'Este Emery, Pr. Feb., 1913, 462.

Notes on the examination of 'smears' of the *S. pallida*.—B.M.J.ii./07 1510.

The development of the halteridium in the mosquito, as found by Schaudinn is doubted.—B.M.J. ii./07,88.

An atlas of 38 plates of Spirochetes has been issued as a memorial of the late Fritz Schaudinn.—B.M.J. i./08,278.

Biochemistry. 'Lipoids' and *S. Pallida* described.—L. i./09,489.

Persistence of disease organisms in the body. In syphilis and tubercle the respective organisms once admitted have their potentiality for mischief terminated only by death of their host. In cancer probably the same condition exists though no causative germ is known.—B.M.J. i./11,973.

**Noguchi's Method of Diagnosis of Syphilis.**—(*Distinguish from the Noguchi modified Wassermann and the Luetin Test*). Boil two parts of the cerebro-spinal fluid with 5 parts of a 10% solution of Butyric Acid in normal saline for a few seconds, then add one part of Normal Sodium Hydrate and again boil briefly. A flocculent or granular precipitate is obtained on standing (in parasymphilitic affections) due to presence of a globulin. The test distinguishes general paralysis from other forms of insanity not associated with meningo-encephalitis.—L. i./09,1666; B.M.J. i./09,1112,1408.

**Luetin Test (Noguchi's).**—A skin test for diagnosis of syphilis. An emulsion of the killed bodies of the Spirochetes (killed by heating to 60° C.) is injected intradermically. The test is analogous with the Von Pirquet reaction. A papular or pustular lesion is formed resembling a small gumma if patient is infected.—B.M.J. ii./13,1100,1106; D'Este Emery, L. i./14,222.

Ampoules are made containing 0.07 Cc. sufficient for one test. The emulsion is sterile and contains 0.5% Trikresol as preservative.

**Complement-Fixation Reaction for the Diagnosis of Syphilis** was first described in Deut. Med. Woch. of May 10, 1906, by Wassermann, Neisser and Bruck. It is an application of the general phenomenon of deviation or fixation of Complement first described by Bordet and Gengou in 1901.

"Complement," (*syn.* Cytase, Lysin, Alexine), which is present in fresh blood serum (whether syphilitic or not), has the power of hæmolyzing, disintegrating or dissolving blood corpuscles, *i.e.*, **Hæmolytic Action**. It is "fixed" in the reaction by the combined action of Specific Amboceptor which is present in syphilitic serum and "Antigen." It can also be destroyed by heating at 56° C. for half an hour.

The original Wassermann reaction is complicated,—in this, for example, the antigen is a saline extract of a syphilitic foetus. Subsequently various workers showed it was possible to employ an alcoholic extract of heart muscle, *inter alia*, in place of this substance, but the greatest simplification so far introduced is the use, notably by



Hecht and Fleming, of the "Complement" and hæmolytic Amboceptor of the serum to be tested, operating with these on sheep's blood corpuscles.

Other modifications are those of Noguchi, Emery, and Wechselmann, which will be considered later.

If Antigen + Syphilitic Serum + Sheep's Corpuscles, be mixed together hæmolysis does not take place.

But if Antigen + Normal Serum + Sheep's blood be used hæmolysis does take place.

Similarly with Syphilitic Serum + Normal Saline Solution + Sheep's Corpuscles hæmolysis occurs.

To follow the last statement one must remember Syphilitic Serum contains Complement as well as Amboceptor, and the Complement was not previously inactivated by adding Antigen.

**Antigen.** (A bacillary product).

Is contained in an Extract of an infected organ, *e.g.*, syphilitic liver. An extractive of an ox heart is now used instead. It has no restraining action by itself on the Complement.

**Amboceptor** (*Syn.* Immune body or Fixative), is formed during immunisation, and has no restraining action by itself upon Complement. These *two* together will, however, inactivate Complement in any Serum and so prevent Lysis.

As *Syphilitic Serum* contains *Amboceptor* and *Complement*, in Hecht's or Fleming's method (*q.v.*) of applying the test the Complement is not previously inactivated, and consequently extra Serum is not required in the test (*vide infra*).

Wassermann employed as Antigen a saline extract of the Liver of a syphilitic foetus, the serum of a rabbit immunised to sheep's red corpuscles as Amboceptor and fresh guinea-pig serum as Complement. The test can be done equally well with saline extracts of normal liver and other organs. Alcoholic Extracts, however, keep better. Alcoholic Extracts of the heart (human, sheep, rabbits, or guinea-pigs) are useful (other substances of a lipoid nature such as Sodium Oleate, Cholesterin, or Sodium Glycocholate will do also, but Ox Heart Extract is the best).

The natural hæmolytic Amboceptor for sheep's corpuscles in human serum was found to be as useful as that of the immunised rabbit which was dispensed with, but the Complement of the guinea-pigs' serum was still required. Hecht made the serum to be tested supply the Complement as well as the Hæmolytic Amboceptor. He employs small quantities in comparison with the test as originally described.

For **Fleming's Method** of conducting the test are required,—

**Antigen** (Ox-Heart Extract):—

Heart muscle 1 Gm. is ground up with 5 Cc. Absolute Alcohol and heated at 60° C. for one hour and then allowed to stand 24 hours at 37° C. The supernatant liquor is poured off and diluted with Normal Saline Solution before use in such proportion that while completely binding the Complement of a syphilitic serum it will not interfere with the hæmolitic power of normal serum. Too large a percentage of Alcohol must not be present, as if used hæmolysis will take place when sheep's

corpuscles are added even in the absence of serum. No extract should be used which requires to be in a strength exceeding 10 %, *i.e.*, Alcoholic Extract 1, Normal Saline 9. The strength of the Extract is tested by taking say 1,  $2\frac{1}{2}$ , 5, and 10% and using each with a syphilitic and a non-syphilitic serum in the manner described. The strength is chosen which will completely prevent hæmolysis with the syphilitic serum, but which will have no effect on normal serum. Heart Extract thus prepared retains its activity for a long period of time.

'Antigen' Sterules are prepared. Another form of 'Antigen' as above mentioned is

**Sodium Glycocholate Solution** but is far less reliable.

Sodium Glycocholate 1, Sterile Distilled Water to 100.

N.B.—This must be fresh, as the solution is favourable to bacterial infection.

Instead of the usual Alcoholic Extracts of Ox Liver or Guinea-pig heart as Antigen it has been found that **Lecithin** and **Lecithin plus Cholesterin** are more sensitive as Antigen.—B.M.J. ii./11,748.

Action of Cholesterin and its derivatives on Lecithin as Syphilitic Antigen and as hæmolysin with Cobra venom.—Jl. Path. Bact., Oct. 1911.

**Washed Sheep's Corpuscles**, from the fresh blood suspended in Normal Saline. Remove fibrin from fresh blood by clotting—rapidly stirring at the time of drawing from the animal. Centrifugalise and pipette off the Serum. (N.B.—A powerful centrifuge is required.)

Add Normal Saline Solution and again centrifugalise several times to free from Complement. Finally dilute with Normal Saline Solution making approximately a 10% suspension.

**Sterules of Washed Sheep's Corpuscles Suspension** are prepared and may be relied upon for a reasonable time.

The Corpuscles can be preserved by adding a small proportion of *o.m.p.* Cresol without affecting the reaction.—Wyatt Wingrave.

*Method of conducting the test.*

In carrying out Fleming's modification of the Test, the first requirements are the bent capsules (Wright's) as full as possible of (a) normal, (b) patient's and if possible of (c) a known syphilitic blood. To fill a capsule break off the tips of same, and after pricking the first or second finger about a  $\frac{1}{4}$  inch away from base of the nail or other convenient place, make the blood flow into the bent end of the capsule by capillarity. This is done by swinging the arm bending down so that the hand is at a level of the foot, winding a bandage several times tightly round first and second joint and intermediate portion of the finger,—then, after pricking, as indicated, with a "flamed" needle, it is possible by flexure to produce a flow of even 5 Cc. of blood if desired. The blood may, if preferred, be collected similarly from the lobe of the ear. Having at least half-filled the capsule, both ends are carefully sealed, avoiding heating the Serum as much as possible, and the Serum is allowed to separate naturally or by the aid of a centrifuge.

Make a file mark round the normal blood capsule just above the level of the Serum and break off carefully. Next snap off the end of an Antigen Sterule and finally treat a "Normal Saline" Sterule in like manner.

Make a small mark on the stem of a long-pointed Wright's 'pipette' (3-inch pieces of  $\frac{1}{8}$ -inch glass tubing drawn out into a 6-inch capillary point and provided with a teat at the thick end) with a paraffin pencil about half an inch from the point. This is termed 1 volume,—a similar mark is made 2 inches from the point indicating four volumes. Draw up with this pipette volumes of the various liquids and introduce into diminutive corked tubes (about 1 inch  $\times$   $\frac{3}{8}$  inch) in a small rack in two rows, as follows:—



	1 volume Control Serum, 4 volumes “Antigen.”	1 volume Syphilitic Serum, 4 volumes “Antigen.”	1 volume Patient’s Serum, 4 volumes “Antigen.”		4 volumes “Antigen.”	
Back Row	B.	D.	F.	H.	J.	X <sub>t</sub>
Front Row	A.	C.	E.	G.	I.	

1 volume Control Serum, 4 volumes Normal Saline.	1 volume Syphilitic Serum, 4 volumes Normal Saline.	1 volume Patient's Serum, 4 volumes Normal Saline.
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Tubes G.H. and I.J., etc., can be used to do two or more patients' sera simultaneously.

Into X place 4 volumes of "Antigen" alone.

In all the above the "Antigen" is to be diluted 1 volume with 99 volumes of Normal Saline in a separate little tube or Cc. measure before taking up the volumes. It may be necessary, however, to vary the strength of this "Antigen" dilution from time to time. Its strength should first be tested by taking various dilutions, say 1 in 100, 1 in 40, 1 in 20, 1 in 12, 1 in 15, etc., and using each with a syphilitic and a non-syphilitic serum—that strength being chosen for conducting the reaction which will completely prevent hæmolysis with the syphilitic serum, but will have no effect on the Normal Serum.

Insert corks and shake the contents of each tube slightly and maintain at 37° C. for one hour. After which add 1 volume of washed Sheep's Corpuscles to each tube, including "X," and incubate again for from 1½ to 2 hours.

The results are then read off, but sharper differentiation is obtained if the tubes are inserted in the ice chest for several hours so as to allow of sedimentation in the non-hæmolysed tubes.

We shall get :—

Hæmolysis in "A," owing to absence of "Antigen" and Specific Amboceptor.

Hæmolysis in "B," owing to absence of Specific Amboceptor.

Hæmolysis in "C," owing to absence of "Antigen."

NO Hæmolysis in "D," because Complement is fixed.

Hæmolysis in "E," owing to absence of "Antigen."

NO Hæmolysis in "F," if patient syphilitic, owing to added "Antigen," otherwise Hæmolysis as in "B."

NO Hæmolysis in "X" should be observed.

Note tubes "C" and "D" are only for control purposes and need not be used in routine work. The process is an exceedingly delicate one, and the original article by A. Fleming (L.M. i./09, p. 1512) should be studied—these notes are only a *résumé*.

In some cases there is a deficiency of Amboceptor to sheep's corpuscles shown by absence of hæmolysis in tube A, C, E, G, or I. If so, repeat the test, but before adding the sheep's corpuscles add a small quantity of hæmolytic Amboceptor in proportion of 1 to 500 of Corpuscles Suspension, and shake. Or, add to each of the tubes containing the serum concerned one volume of Normal Serum (heated to 56° for 10 minutes), which is known to have a hæmolytic power for sheep's corpuscles. This deficiency, however, only occurs in about 10% of cases.

In a very few cases the addition of Complement may also be necessary. This can be done by adding same in the form of guinea-pig's serum containing Complement only or fresh human serum containing both Complement and Amboceptor before the first incubation period. Thus one puts in one tube (F) 4 volumes of "Antigen," 1 volume of patient's serum and 1 volume of fresh Normal Human Serum, while in the control tube "E" the "Antigen" is replaced by Normal Saline Solution.

In our hands Fleming's method has given good results. We tried a large range of dilutions of the Concentrated Antigen Solution, 1, 1½, 2½, 5, 7½, 10, 12½, 15 and 20% in Normal Saline. About a 4% Dilution was found to give the best result, but the strength requires standardising from time to time.

The following is an abstract of an account by Prof. Muir of the research leading up to the reaction :—

“The story really concerns the anti-substances which appear in the blood as the result of immunisation, and the first step was made with the discovery of antitoxins, first in the case of tetanus, and a little later in the case of diphtheria. These were the first known anti-substances, and we now know that they combine with the corresponding toxins so as to form a substance inert towards the cells of the body ; beyond this neutralising action they have, so far as is known, no other effect. It was, however, shown later that a great many bodies other than toxins, such as ferments, bacteria, serum, milk, or cells of another species, might give rise to anti-substances when injected into an animal, and all such substances are now generally known as *antigens*, on account of this property. In some instances the anti-substance produced some distinct and easily recognised change when allowed to interact with the corresponding antigen. For example, when an animal was treated with injections of foreign serum, the anti-substance developed might lead to the formation of a precipitate when added to the antigen, hence it was called a *precipitin* ; or again, when bacteria, were used in the injections, the anti-substance might cause clumping or agglutination of the corresponding bacteria, and hence was called an *agglutinin*. The study by Pfeiffer of the serum of animals highly immunised against the typhoid or cholera organisms showed that the increased bactericidal action possessed by their serum was due to two substances, of which one was specially developed in the process of immunisation (an anti-substance), and the other was present in the normal serum ; the former is now known as an *immune-body*, *amboceptor*, the latter as *complement* or *alexine*. Further researches have shown that in all cases where a dissolving action is developed during immunisation, two corresponding substances are concerned. For example, when an animal is injected with the red corpuscles of another species, its serum acquires remarkable hæmolytic properties towards such corpuscles ; if the serum be heated at 55° C. for an hour, the hæmolytic property is lost, because the complement is destroyed at that temperature, but it is restored on the addition of fresh normal serum containing complement. It follows from this that corpuscles treated with the corresponding antiserum, heated to destroy complement, serve as a test for the presence of complement ; if complement is present, the corpuscles will undergo lysis ; if complement is absent, or has in some way been used up, the lysis will not occur. There are two other points to be noted. The first is that each anti-substance is specific (within certain limits) ; that is, each anti-substance exerts its effect only against the antigen which has led to its production. The other is that anti-substances are formed not only in response to an artificial inoculation, but are developed in the course of an attack of the natural disease : in other words, during the latter a process of immunisation, attended with the formation of anti-substances, appears to be going on. Accordingly, in the serum-diagnosis of disease we test for the presence of the anti-substances to the particular bacterium, and of these the two chief varieties usually considered are the agglutinins and the immune-bodies. As is now well known, the presence of the former is shown by the clumping of the causal bacterium, which occurs on the addition of the serum in suitable dilution from a case of the disease, to an emulsion of the bacterium ; with regard to it nothing more need be said. How can an immune-body be demonstrated ? The answer is, that immune-body, along with the corresponding bacterium, will lead to the using up or fixation of complement, and thus interfere with the lysis of sensitised corpuscles when these are added to the mixture. This reaction is often known as the “ Bordet and Gengou phenomenon,” *c.f.* also p. 355, inasmuch as these observers showed that the injection into animals of a great many different substances as antigens—bacteria, foreign proteins, milk, etc.—gave rise to immune bodies, each of which, in association with the corresponding antigen, fixed complement, and thus prevented the lysis of sensitised corpuscles.

“Now with regard to the complement test as applied to syphilis. After the *spirochæta pallida* had been discovered by Schaudinn and Hoffmann 1905, and established by further researches as the cause of the disease, it seemed only reasonable to enquire whether the deviation of complement reaction was given by the serum of syphilitic patients. The observation was first made by Wassermann, Neisser, and Bruck in 1906, and it was found that the phenomenon in question really occurred. Their method was to make a watery extract of a congenital syphilitic liver, which was very rich in spirochætes, to serve as antigen (seeing that, of course, a culture of the organism has not been obtained), and the effect of a mixture of a small quantity of this extract and of syphilitic serum



on guinea-pig's complement was tested; the result, as stated, was that complement was fixed, whereas with serum from other than syphilitic cases this did not happen. Apparently, then, in syphilis, just as in various bacterial diseases, a specific anti-substance (immune-body) could be demonstrated in the blood. The subject assumed, however, quite another aspect when a little later it was found by Marie and Levaditi that an extract of normal liver and of other organs could be substituted for the extract of syphilitic liver, or in other words could take the place of the supposed antigen; alcoholic extracts are specially suitable for the purpose. Further observations showed that solutions or suspensions of substances of definitely known constitution, such as glycocholates, oleates, lecithin, and other lipoids, could be used in place of syphilitic extracts, that is, when mixed with a syphilitic serum, fixed complement. Thus, the application of the principle of the deviation of complement by an antigen and its anti-substance, as demonstrated in the case of bacterial diseases, has led up in the case of syphilis to the discovery of a phenomenon of a different nature. All that we can at present say regarding the Wassermann reaction is that there is present in the serum of syphilitic subjects a substance, *probably a modified protein, which, in the presence of other bodies, especially lipoids, leads to the fixation of complement and that this reaction constitutes the most valuable method of diagnosis which we possess.*—R. Muir, *Glasg. Med. J.* Nov. 1910.

The original Wassermann Test is conducted as follows:—“About 10 Cc. of blood are removed with a syringe from a vein at the bend of the elbow, and transferred to a sterile test-tube. The serum is allowed to separate spontaneously from the clot; before use it is heated for half an hour at 57° C., then a fixed amount of the serum (0.05 c.c.) is added to a series of small test-tubes in which the fixed amount (0.6 Cc.) of emulsion of organ extract has already been placed (the organ extract is made by macerating one part of minced organ—ox liver or heart—in four parts of 96% alcohol for twenty-four hours; the emulsion is made by adding one part of extract to five parts of saline). Varying amounts of complement—normal guinea-pig's serum—are added to the series, and after one and a half hour's incubation at 37° C., the test blood suspension is added—1 Cc. of 5% suspension of washed ox's blood corpuscles sensitised with five doses of immune body from the rabbit. After further incubation for one hour at 37° C. the result may be read. Three control series are always set up at the same time as the experiment, *viz.*, (1) the patient's serum (0.05 Cc.) in saline; (2) the organ extract emulsion (0.6 Cc.) by itself—to these two series complement is added so as to estimate the inhibitory effect of each of these reagents by itself on the complement; (3) varying amounts of complement are added to saline to estimate exactly the hæmolytic dose of complement. These series are incubated at the same time as the experiment, and they also receive sensitised blood suspension.

“The result is positive when the mixture of patient's serum and organ extract absorbs five or more doses of complement in addition to the amounts absorbed by each reagent alone. Thus, supposing that the patient's serum by itself absorbs one dose of complement and the organ extract emulsion by itself absorbs two doses, then the mixture of serum and organ extract must absorb at least eight doses of complement, as shown by absence of hæmolysis of the test corpuscles in the tube to which this amount of complement had been added, if the reaction is to be counted positive.

“The criterion of a positive reaction is based on the result of the examination of a large number of known syphilitic and non-syphilitic sera. In practice, a number of factors must be taken into account. Thus, the physical state of the emulsion of organ extract is of importance. A turbid emulsion made by floating the alcoholic solution on to the top of the saline and then mixing slowly is much more efficient in eliciting a positive reaction with syphilitic sera than is a clear emulsion made by mixing rapidly the same amounts of alcoholic extracts and saline. Again, the complement-containing serum obtained from different guinea-pigs shows individual variations, some animals yielding complement which is much more readily deviated than others. Provided that the examination is always controlled by testing at the same time as the patient's serum a known negative serum, there is no danger of obtaining an erroneous positive reaction with a non-syphilitic serum. On the other hand, a weakly positive serum may be overlooked on a single examination, but a repetition of the test will usually clear up the diagnosis.

“The reaction is essentially a quantitative one, as it depends on an accurate estimation of the amount of complement absorbed by a mixture of organ extract and serum as compared with the amounts absorbed by each reagent alone.

"Browning, Cruickshank, and M'Kenzie's modification depends on the fact that the amount of complement absorbed by a mixture of serum and lecithin is increased on the addition of cholesterin if the serum is syphilitic; but not if the serum is normal. Accordingly, two series of tests are carried out simultaneously—in the one, complement is added to the mixture of serum and lecithin; in the other, to the mixture of serum, lecithin, and cholesterin. If more complement is absorbed in the second series than in the first then the reaction is positive."—C. H. Browning, Glasgow Med. Jl. Nov. 1910.

### **References to the Original Wassermann Method.**

The test is of value where no spirochætæ are found.—L. i./09,481.

Doubts whether lipoids alone responsible for the test—if so they must be present in enormous excess. Unlikely that such a pathological cell activity should only be found in one infection. Wassermann's Technique followed in the main. No difficulty in obtaining the 2 Cc. of patient's blood necessary. The objection to Bauer's method of making use of the amboceptor normally present in human serum in place of sheep's corpuscles, is that the natural amboceptor varies considerably and in a few cases is practically absent, so that the serum of such an individual could not be tested by the method.—149 cases. L. i./09,1515.

The original Wassermann Test regarded as specific and reliable. Especially useful when applied to the cerebro-spinal fluid for diagnostic purposes.—Mott. B.M.J. i./09,461.

Wassermann's (original) test.—For a good description see B.M.J. ii./12,1504.

Wassermann could report 1010 non-syphilitic serums examined without a single positive result. Spinal fluids from 64 cases of general paralysis and other diseases examined at Mott's request—59 of the 64 gave positive result—clinical evidence connecting tabetic and general paralysis with syphilis. Method employed essentially Wassermann's but ox blood corpuscles used instead of sheep's.—Henderson Smith and Candler.—B.M.J. ii./09,198.

Positive reaction (original Wassermann) in scarlatina the exception not the rule.—B.M.J.E. i./09,28.

Wassermann's original employed—to be regarded as specific. Necessity for obtaining a comparatively large amount of serum overcome by diminishing amounts of reagents used. With regard to Antigen aqueous extract of a liver rich in spirochetes is best. Some difficulty in interpreting results. Discussion of reliability of the test and theoretical considerations. A lengthy article with bibliography of 74 authors.—B.M.J. ii./09,1019.

Plaut (The Wassermann Sero-diagnosis of Syphilis in its application to Psychiatry) comes to the conclusion that *the original Wassermann's method is alone to be trusted.* With regard to general paralysis he considers it important to test both serum and spinal fluid.—B.M.J. ii./11,760.

### **References to Fleming's and other Modifications.**

A. Fleming on Syphilis and the Wassermann Reaction.—P.R.S.M.—Surgical Sectn., July, 1910, 219.

Objection has been raised to Fleming's and allied methods to the effect that 'hæmolytic power for sheep's corpuscles was not found in 30% of human serum, and that in 22 known cases of syphilis the reaction had not been obtained in half the number. Fleming has quoted other workers as having found 10% failures. Clemenger finds in 500 observations only 5% which did not possess hæmolytic action—does not think this will detract from value of the reaction—any deficiency can be supplied by adding a small amount of normal hæmolytic serum in these cases. Clemenger finds that 'in practically all cases of syphilitic lesions, whether primary, secondary or tertiary, a positive reaction can be obtained providing suitable heart-extract is used.'—B.M.J. ii./09,575. See also *ibid.* p. 917.

'Solving the problem of half a dozen variables.' Advances are being made that will speedily bring the test into daily use. No one has projected a simpler rationale than Fleming—room for further simplification of Flashman and Butler's method.—B.M.J. ii./09,1087.

### **Fleming's Method of Conducting the Wassermann Reaction discussed**

Fleming has practised his modified method on 12,000 samples during three years. The number of Sera that do not possess any hæmolytic power for sheep's corpuscles is well under 10%. Sometimes the Salt Solution may be at fault which destroys the hæmolytic power during the first incubation period.—L. ii./12,115,183,259,336.



Fleming's method upheld. P. N. Panton states the Serum should be examined within 12 hours of being taken and should be stored on ice. It is important to wash the sheep's corpuscles thoroughly.—L. ii./12,48.

In the Fleming Test the blood should be examined soon after being taken. The Antigen should be controlled both by normal and syphilitic sera. A record of many cases appears in favour of the Fleming method (a syphilitic liver Antigen employed).—P. W. Bassett Smith, L. ii./12,558.

2,500 Wassermann reactions, using Fleming's modification. Quantitative tests employed by using graduated dilutions of Antigen. Thus supposing satisfactory dilution to be 1 in 15, dilutions of 1 in 30 and 1 in 60 also. It is found that by washing the sheep's corpuscles six times, thrice with Citrated Saline and then thrice with 0.85% Saline and by taking the blood from the patient on the morning of the test, a very small percentage of blood fails to give a readable result.—L. Kilroy, L. i./13,304.

The reaction (Fleming's method) in syphilis becomes + in about 3 to 4 weeks after appearance of the sore in most cases.—B.M.J. ii./13,1345.

Browning and Mackenzie's modified method. 125 out of 135 cases of syphilis gave positive reaction, and 107 out of 108 with no evidence of syphilis, gave negative results. The control cases included a large variety of acute diseases—pneumonia, enteric, scarlet fever, etc.—L. i./09,1521.

Wassermann's reaction generally accepted not specific, and that it is more probably an increase in the lipoid content of syphilitic serum rather than the interaction between a specific body and an Antigen that produces the complement fixation,—possibly this substance is present in all sera and that there is a marked excess in syphilis. Did not obtain such clear results when depending on the hæmolytic action of human serum instead of adding special hæmolytic serum. 200 tests employing rabbit's heart extract. Neisser technique modified employed. Reaction not due to Mercurial treatment.—L. i./09,1523.

Porges' modification of Wassermann (using Sodium Glycocholate). Positive reaction is definite evidence of past syphilitic inoculation.—Harry Campbell.—B.M.J. i./09,567,640.

Wassermann modified by using for Antigen dried syphilitic congenital liver. Primary cases marked reaction. All cases of early secondary syphilis positive results; in late secondary or tertiary manifestations results more variable. 50% of para-syphilitic cases positive reaction.—B.M.J. ii./09,325,377.

The test is useful in the diagnosis of secondary and tertiary syphilis, but not in cases of early chancres.—Pr., Oct. '10,430; J. McDonagh, Pr., Sept. '09.

With regard to Wassermann's reaction MacDonagh (Pr., Nov., 1910, p. 671) writes as follows:—

'It was my custom to employ both active and inactive patients' serum, one serving as a control against the other; the reason for so doing was owing to the fact that in inactivating the serum at 56° C. for half an hour, complementoid bodies were formed which had the power of acting like complement, causing thereby a negative reaction in one which should have given a positive. *Wechselmann* ingeniously showed that these complementoid bodies could be precipitated by barium sulphate, his method of procedure being as follows:—0.9 Cc. of inactivated serum is mixed with 3 Cc. of physiological saline solution and 0.5 Cc. of a 7% fresh precipitated barium sulphate saline emulsion, the mixture being well shaken, then put into an incubator at 37° for an hour, it is then centrifugalised and 1 Cc. is used for the reaction. The barium sulphate acts probably mechanically, and it matters little whether more than the above quantity is used.' This method should be used, 'since it not infrequently happens, that an undoubted case of syphilis, especially in the late stage of the disease and not under the influence of treatment, gives a negative reaction in the ordinary course of events and a positive with the barium sulphate prepared serum.'

Although this addition adds considerably to the labour, it, at the same time, by increasing the positive results in syphilitic cases, enhances the value of a negative reaction. The best antigen is that prepared from a syphilitic liver, and, contrary to what serves for Wassermann's reaction, an extract of a normal organ, be it human or animal, is useless. It is extremely doubtful whether this test will become generally employed and prove of diagnostic value, but, nevertheless, it is a step in the right direction, since we cannot rest in peace until we have probed the foundations of the Wassermann's reaction."

**Stern's Modification** has its uses. The original Wassermann being less sensitive, is less likely to mislead in diagnosis, while the more sensitive modification of Stern is more likely to give early evidence of retrogression and of the necessity for further treatment.—B.M.J. ii./II 686,693.

**Noguchi's Modified Wassermann's Test** is thought to be neither simpler than the original, nor an improvement on it. The use of human amboceptor is fraught with the danger that antibodies active to human albumins may act inhibitorily on the hæmolysis.—Deut. Med. Woch. 26, 1910, per B.M.J.E. i./II, 52. The reader is referred to Noguchi's Book on the subject for the technique.

#### W. D'Este Emery's Method.

Many fatty substances, *e.g.*, Lecithin, produce the same result as when Antigen is used. The substance in the serum is therefore not a true antibody, and it is, moreover, not specific, since it occurs in other diseases, and in normal serum, but in syphilis it is in excess,—hence the importance of a quantitative method of application.

All sera give some absorption of complement with liver extract if the latter be strong enough. The reaction, *may in fact be explained somewhat* as follows: The dilution of the alcoholic fatty solution produces an emulsion of fine particles. Syphilitic Serum contains a substance with power to combine with these, and in so doing alters in some way the surface tension between them and the fluid in which they are suspended,—hence they clump and in doing so *attract to themselves any complement which may be present in the fluid*. The reaction is therefore partly physical and partly chemical. Note that antigen changes in strength (as a rule becoming stronger) also that the diluted extract is more turbid and has a more powerful action if the two fluids are allowed to mix gradually and not mixed at once. One or other proceeding must always be used. Emery floats the Alcoholic Solution on top of the Saline and allows it to diffuse gradually 10 minutes, and then slowly stirs them together.

In the original Wassermann and other modifications the complement originally present in the Serum is destroyed by heat at 55° or 60° C. Emery thinks this may hide the ultimate reaction—possibly by linking together the complement and some of the so-called syphilitic antibody. The explanation usually given for first eliminating complement and then adding it in the form of guinea-pig serum is that the amount in human serum varies so much as to make the test unreliable. Emery thinks this explanation unsatisfactory,—the complement added is in no way known or estimated. Some workers dry the complement on filter paper,—this must be inaccurate. It is true some methods attempt evaluation of complement, but the process is lengthy and the estimation is probably of little use the next day. Emery uses unheated serum and fully sensitised human corpuscles,—this will work with even a trace of complement.

From results it is clear that the presence of large amount of complement does not vitiate results. The hæmolytic system is simply an indicator analogous with the use of litmus in titration. Emery objects to the use of sheep's corpuscles. Amboceptor is not always present (or not in sufficient quantity) in human serum to link up with its complement to these corpuscles. Hence non-syphilitic serum has to be added, but the *amount* to add is not easy to say. Human corpuscles are used in Tschernugobow's, Noguchi's, Birt's and Emery's processes—they involve the use of an immune serum to supply the necessary amboceptor to link up the pre-existing complement.

**Emery's Method** is as follows:—Prepare an emulsion of sensitised washed human corpuscles by adding 1 volume of corpuscles to 4 volumes of heated immune serum from a rabbit which has been injected with human corpuscles. This serum must be strong enough to sensitise the corpuscles to a trace of complement, and not strong enough to clump them instantly. The dilution is found experimentally and the serum diluted accordingly. Enough of this 20% emulsion of corpuscles is prepared to last for about 20 tests. The mixture is incubated a few minutes to allow of the linking up of the amboceptor and is then ready for use.

In the test 1 part of serum to be tested is mixed with 4 parts of Saline Solution (about 5 C.mm. in all by means of Wright's capillary pipettes) Place in water bath at 38° C. ; next a mixture with diluted antigen in the same proportion is placed alongside,—this being the test, the other the control. Other sera to be tested can be placed alongside in the customary manner. The combination takes place in five minutes or less—there is no need to wait



the customary hour. Next add 1 volume of the Emulsion of sensitised corpuscles to each tube—mix up thoroughly. If the balance between amboceptor be right, the corpuscles in the control will be dissolved before they have time to settle, and if not they must be stirred once or twice,—the actual 'test' tubes being treated likewise. In a few minutes the results can be read. In a *negative reaction both tubes show haemolysis*, complete or nearly so; in a *positive one the first tube only* shows it, whilst in the latter the corpuscles will settle leaving a colorless supernatant fluid. With regard to **Standardisation of Antigen** this should be compared with *normal* not with syphilitic serum. Emery advises and *suggests as standard* the use of an extract of such strength that when diluted 10 times its volume it exerts a definite inhibiting influence on a normal serum, but does not cause complete inhibition except in a small proportion of cases,—*Normal Human Heart Muscle* is used. The extract is prepared 1=1 with Absolute Alcohol (see paper. L. i./II, p. 567, for details) also for details of the **Quantitative Method** to which justice cannot be done in a short abstract.—L. ii./Io, 732; i./II, 564, 594.

W. D'Este Emery provides further details of his method, which he says is as accurate as it is possible to make it.—L. ii./12, 183.

Von Dungern introduced a modification of Wassermann's Test.

In this method the complement is provided in strips of filter paper, soaked with guinea-pig serum and dried. The antigen is an extract of guinea-pig heart, dissolved in alcohol. The immune-body is contained in the serum of an animal treated with injections of human red blood corpuscles. The test is carried out as follows:—Two test-tubes are filled each with 2 Cc. of normal saline, to one of these a drop of antigen is added. A piece of the complement-paper is then added to each. A few drops of the patient's blood is put into a watch-glass, stirred by means of a match until it is defibrinated, and 0.1 Cc. added to each tube. After an hour a little immune-serum is added to each tube. If the patient is syphilitic, the red corpuscles in the test-tube containing antigen are agglutinated in a few minutes and sink, while the supernatant liquid remains clear. In the other tube, the red corpuscles remain suspended and soon become dissolved, forming a bright red solution. If the patient is not syphilitic, the contents of the first tube also behave like that of the second one. The method is said to be delicate.—Münch. Med. Woch. Mar. 8, 1910; per Pres. Aug. 1910.

### *Parasyphilitic Conditions in Relation to the Reaction.*

Parasyphilitic conditions, as instanced by tabes and general paralysis vary somewhat. General paralytics give positive results in every case,—tabetics do not give it in more than 60%. Most of those who failed to give the reaction denied all history of syphilis. When energetic treatment has produced a cure the patient will fail to respond to the test. Time will show whether this is the case,—if so the test will be of very considerable value.—B.M.J. i./09, 1238; ii./09, 984; L. i./09, 1457, 1512.

Cytodiagnosis, lymphocytes markedly increased in 80 progressive parasyphilitic affections.—Mott. L. i./09, 489, 1354, 1666; B.M.J. i./09, 1408.

Differential diagnosis of syphilis and parasyphilis of the nervous system. The doctrine has been put forward that "general paralysis is, like tabes, a consequence of syphilis, and that the two diseases are so similar in their etiology that they might probably be regarded as one disease affecting different parts of the nervous system." Others have said that "General paralysis is the product of syphilisation and civilisation." Practically every case of general paralysis gives a positive lymphocyte and a positive Wassermann reaction.—F. W. Mott. B.M.J. ii./II, 1337; L. ii./II, 1392.

Syphilis of the nervous system. The cerebro-spinal fluid of 127

cases of varied forms of insanity examined for Wassermann Reaction. 64 of these were general paralysis, and in 59 or 92·1% a positive result was obtained. 21 of the 59 since dead from general paralysis.—Mott, P.R.S.M., Neurol. Sectn., Feb. '10, p. 35 *et seq.*

Wassermann Test in general paralysis. The reaction is one of the most reliable and valuable tests for general paralysis. A positive reaction was obtained with the cerebro-spinal fluid in 90% of cases. The Liver Extract was made in this investigation slightly different from the original. The liver was reduced to an anhydrous powder by mixture with Plaster of Paris and silver sand—then washed with Acetone and finally extracted with cold alcohol,—this was thought to eliminate substances adversely affecting the test.—L. ii./11,1320.

The spirochete of syphilis, it is stated, actually flourishes in the brain in general paralysis and is present in, at least, some cases of locomotor ataxia.

Of 204 idiots examined in America 30 or 14·7% gave the + Wassermann Reaction (Roy. Soc. Med., Debate on Syphilis.—B.M.J.ii./12,70.

Mental Disease, 150 cases.—In a number of cases of general paralysis the blood and cerebro-spinal fluid may give a negative Wassermann reaction even on repeated examinations. This does not agree with McIntosh and Filde's statement that "a negative reaction in serum in a suspected case of general paralysis will render this diagnosis improbable"; and "a negative reaction in the cerebro-spinal fluid of a general paralytic is unusual." A negative Wassermann reaction is more likely to be obtained in the case of a female general paralytic than of a male. The blood is negative rather more often than the cerebro-spinal fluid in the case of male patients, but the reverse obtains in the case of female patients. At least 0·1 Cc. of serum should be used for the test, and, where practicable, 0·2 Cc. should also be used. At least 0·5 Cc. of cerebro-spinal fluid must be used, if possible also 0·8 Cc., otherwise positive results may be missed. Practically the original Wassermann Test employed.—David Nabarro, B.M.J. ii./12,1454.

### *General References to the Reaction.*

In cardiac disease. Positive reactions in a number of cases seemed to indicate that syphilis is an important factor in the production of cardiac disease.—L. ii./09,1159.

Ehrlich showed that hæmolytic amboceptors can be developed in the serums of animals injected with the red corpuscles of other animals of the same species. Experiments by Batty Shaw show that it is possible to develop in the serums of animals into which injections have been made of the organs of another animal of the same species, in part at least an increase of the hæmolytic power of the serum. *Emulsions* of different organs seem to have varying power of checking hæmolytic power of these experimental serums,—kidney emulsion most and liver least.—B.M.J. ii./09,1268.

Wassermann's Reaction with cerebro-spinal fluid. A positive reaction is obtained when the blood or cerebro-spinal fluid causes fixation of complement of guinea-pig serum. A reliable aid to diagnosis.—F. W. Mott, L. ii./10,82.

A large proportion of dead bodies gave the reaction—not necessarily attributable to syphilis. It is not of value on such as diagnostic.—L. ii./10,204.

Blood Serum of Idiots examined.—15% gave the reaction. Not unreasonable to assume a casual relation between syphilis and idiocy.—L. ii./10,227.

*Failures of the Reaction.*—Mistakes are more often due to defective system of applying it than to the method itself. Warning against neglecting the clinical symptoms and relying exclusively on the results of the Wassermann's reaction.—L. ii./10,263.

B.M.A. (1910) DISCUSSION ON COMPLEMENT DEVIATION METHODS IN DIAGNOSIS, Prof. Wassermann's paper—B.M.J. ii./10,323,1427. H. W. Bayley on the practical value of the reaction, *ibid.*, p. 1430. R. Muir on Fixation of Complement in general *ibid.*, p. 1430. J. Henderson Smith on the Structure of Complement in relation to deviation, *ibid.*, p. 1433. T. W.



Bassett Smith on Diagnosis by Complement deviation, *ibid.*, p. 1434. Ivy McKenzie on Individual properties of Complement and organ extract, *ibid.*, p. 1435. H. R. Dean on comparison of the Original Method with some of its Modifications, *ibid.*, p. 1437. L. W. Harrison on Guidance afforded, *ibid.*, p. 1438. C. H. Browning on Lecithin and Cholesterin as Reagents, *ibid.*, p. 1439. J. O. W. Barrett on Complement Deviation in relation to carcinoma *ibid.*, p. 1440. Leader, *ibid.*, p. 1450.

Useful in determining the specific nature of atypical lesions,—*e.g.*, apparently non-syphilitic soft sores, of extragenital sores and of manifestations of the disease where primary and secondary symptoms had been suppressed. As a means of diagnosis the reaction is supplementary to the examination for spirochetes, and where these are scanty, as in tertiary lesions, it is available alone.—L. ii./10,1491.

In 5 cases of phthisis the only sign of syphilis was a + reaction discovered after death. At the necropsy the condition of the lung was suggestive of old syphilis. This seemed to support the view that syphilis affecting the lungs predisposes to phthisis. Post-mortem examinations in general give a correct diagnosis in non-syphilitic cases. As a rule if the reaction is + during life a syphilitic area will be found post-mortem.—B.M.J.E.iii./10,20, *q.v.*, for further data on these lines.

Association between syphilis and cancer of the stomach. The surgeon should avail himself of the Wassermann Test before exploring the upper abdomen. Syphilis is stated to be a commoner cause of disease than is at present recognised. A not inconsiderable number of cases simulating cancer of the stomach are thought to be the result of syphilis.—B.M.J. ii./10,952.

Boas records 1064 control observations on normal individuals and on cases of other diseases than syphilis. Of these only one case,—one of scarlet fever—gave a positive reaction. In countries other than tropical ones the reaction is specific. He regards the test as not infallible in the first stage of syphilis. In secondary and tertiary syphilis it is infallible provided patient has not previously undergone any treatment. The reaction in general is far more marked in cases which have not been treated than in those that have. In latent syphilis only a + reaction be taken as of any diagnostic value. In general paralysis of the insane a + reaction occurs constantly with serum, also almost always with the cerebro-spinal fluid.—L. ii./10,1705; B.M.J. i./11,1432.

Comparative value of the various methods of antisyphilitic treatment as estimated by the Wassermann reaction. Salvarsan first, inunction or intramuscular injection of insoluble Mercurials second, Mercurial Pills and Suppositories a "bad third."—L. ii./11,1332.

The fallacy of the Wassermann Reaction is that when it ceases to be positive in the secondary stage, it does not signify that the syphilis is cured, but only that *Sp. Pallida* has retired from the blood into the tissues from which they may merge later and give rise to fresh symptoms.—L. ii./13,1225.

Significance of the Wassermann Reaction in gynaecological practice. In gynaecological ailments, especially those associated with uterine hæmorrhage, syphilis, it is stated, is very frequently present. Whenever there is metro-rhagia or menorrhagia apart from obvious cause, such as tumour, syphilis should then be suspected.—B.M.J. ii./13,1003.

Prostitutes—104 girls aged 14 to 18—half of whom resided in the poorest quarters, while the other half lived in the best districts,—all showed a + Wassermann reaction. Apart possibly from a certain proportion of congenital cases infection must have taken place recently and, therefore, all must have been in a highly infective state. Syphilis and the health of the community.—C. H. Browning, B.M.J. i./14,77.

### ***Influence of Drugs on the Reaction.***

In two lectures on 'Recognition, Treatment and Prophylaxis of Syphilis,' Major French deals with all the recent developments. Effects of treatment on the Wassermann Reaction by Mercurials, Salvarsan and Iodide are specially entered into. The value of the Wassermann Test as diagnostic is most critically surveyed.—L. i./11,1315,1316,1386.

Potassium Iodide and the early Arylarsonates (Atoxyl, Soamin and Orsudan) seem to have little, if any action on the Wassermann reaction. Tables showing effect of treatment by intramuscular injections (Mercury) and '606.'—H. W. Bayley, Q. Jl. Med., Jan. 1911, p. 233.

Congenital Syphilis irrespective of treatment, tends to give a + Wassermann Reaction, which is not altered, however much Mercury is given.—McDonagh, P.R.S.M.—Nov. 1910, Otol. Sectn. p. 22.

Emery finds that in the early part of the primary stage a — result is of value, but a reaction may be expected if the supposed chancre has been present for six weeks or more. Children and adults with hereditary syphilis usually give strong reactions. In the later stages if the reaction is present the patient is not cured. If there is no reaction it is difficult to decide, but if a reaction has been present, and is subsequently, the probability of cure is great, but **Mercury itself inhibits the reaction.**—L. i./11,595.

Casoni took sixteen individuals, twelve of whom were definitely non-syphilitic, and four suffering from syphilis, and observed their reaction to the test before and after giving the following drugs: Iron Citrate, Sodium Arsenate, Strychnine, Guaiacol, Sodium Glycerophosphate, and Quinine. In the twelve non-syphilitic cases the Wassermann reaction was negative both before and after treatment. In the four syphilitics one remained unaffected by treatment, the reaction being positive all the time. Of the remaining three, in one the reaction disappeared completely under arsenic, and in the other two it was much less marked. Quinine abolished it entirely in one, while it did not modify it in the others. It was only the quinine and arsenic which modified the reaction, and this not in every case. Iron, Strychnine, Guaiacol, and Glycerophosphate had no effect in this respect.—B.M.J.E.i./11,24.

**Provocative Test.**—Patients giving negative Wassermann Reaction will yield a positive reaction after a Salvarsan injection.—Wyatt Wingrave.

**Serum for Examination, transmitted from abroad** must be collected, under aseptic precautions, transferred to a sterile vessel, inactivated at 56° to 60° C. for  $\frac{1}{2}$  hour and sent in cold storage.—B.M.J. ii./10,240. Or proceed thus:—

**Examination of Dried Serum.**—The blood is collected in the usual way in a bent Wright's Tube, and allowed to coagulate. A definite quantity of the Serum is pipetted off and allowed to dry on blotting paper. This can then be treated with Normal Saline and made up to its original volume for conducting the test.

#### **Hermann-Perutz Reaction.**

Solution No. 1 Sodium Glycocholate 2 Gm., Cholestrin 0.4 Gm., in 100 Gm. of 95% Alcohol. To be diluted with 20 parts of water before use. Solution No. II. 2% Aqueous Solution of Sodium Glycocholate.

The test consists of inactivating the Serum to be tested at 55° C., for half an hour and to 0.4 Cc. of this, adding 0.2 Cc. of Solutions No. I. and No. II. A flocculent precipitate forming at ordinary room temperature indicates + reaction. Supported by Wassermann results.—B.M.J.E. ii./12,52.

### **GENERAL REFERENCES TO SYPHILIS.**

Auto-inoculation and re-infection of syphilis.—J. Hutchinson. L. i./09, 1509.

Syphilis.—History of, on the Wassermann Reaction and Parasyphilis and on treatment. Permanent cures known of Mercurial treatment. Need of a system of registration of syphilitics in the United Kingdom, and of instructing the public.—Sir H. Morris, L. ii./12,497.

Cattle are immune to *Sp. pallida*.—Boxwell, Dublin, Jl. Med. Sci. Dec. 19 12.

#### **Royal Commission on Venereal Disease.**

The paper deals with: Syphilis of the innocent; is syphilis increasing? Modifications of syphilitic phenomena, Notification and regulation, and the example of Australia.—Sir Malcolm Morris, L. i./13,1817.

The pressing need of the inquiry. Legislative reform urgently needed.—Editorial. L. ii.,13,1128.

The danger of syphilis to the community and the question of State control.—H. C. French, L. ii./13,990.

Evidence by Sir V. Horsley and Dr. Florence Willey.—B.M.J. i./14,923.

#### **Antivenereal Campaign in Germany.**

The German Society for combatting venereal diseases founded by Professor Blaschko and Neisser in 1902, has made enormous progress. Over six million warning leaflets suited to either sex have been issued by the Society, —they are designed to throw light on the hidden dangers of loose living.



The information is compressed into ten short rules, which can be digested by the least intelligent and which are designed to contradict certain popular fallacies, as for example, that it is harmful to a man's health to abstain altogether from sexual intercourse.—B.M.J. ii./13,1174.

**Query's Serum.**—*Dose.*—Injection, subcutaneously or intramuscularly of 25 ampoules one a day for 25 consecutive days, ordinarily it is not necessary to renew the treatment. This preparation is made by immunising animals with a 'polymorphous bacterium' isolated from a syphilitic affection. The animal employed is the monkey, as this animal presents a natural resistance to syphilitic affections. Normal serum of monkeys gives a negative Wassermann reaction, whilst the serum of monkeys which have received injections of toxins gives invariably positive.

The Serum is obtained from the carotid of the animal without added preservative. It forms a yellowish liquid, becoming turbid at 45° and coagulating completely at 75° to 80°. It is not to be exposed to temperature above 40° to 45°, which destroys all or part of the antitoxin.

For a patient above ordinary adult weight a larger quantity of the serum than 25 ampoules will be necessary, on the other hand for children 15 to 20 ampoules ought to be sufficient. Syphilitic affection of old standing may well have series of 10 injections after three or six months. Said to be harmless and not painful. Slight local erythema may occur, which disperses in 40 to 48 hours. Ampoules which are turbid are not to be used. Also supplied in *dry form*, each vial of dry serum corresponds to an ampoule of the liquid,—dilutions being made with cold boiled water.

**Tick Fever.**—Muir and Ritchie state that *Sp. Obermeieri* was discovered in 1873 in the blood of patients suffering from relapsing fever (*q.v.*). The so-called African tick fever has been shown to be caused by Spirochete of closely similar character, but bacteriologists (*i.e.*, Muir and Ritchie) are in the habit of keeping the two diseases separate,—associating tick fever with *Sp. Duttoni*. Dutton and Todd in the Congo Free State also Greig and Nabarro in Uganda, 1903, and Milne and Ross in 1904, worked especially on this subject. Clinically the fever closely resembles relapsing fever, but the periods of fever are somewhat shorter—rarely lasting more than two or three days. The organisms are much fewer in the blood than in the European relapsing fever. Morphologically they are almost the same.

The spirochete of this and relapsing fever (Leishman).—L. i./07,806.

*Sp. Duttoni* can be maintained virulent for wild mice in artificial media for 40 days. It will multiply and can be successfully transferred in artificial media—Egg Yolk in mouse decoction was the most successful medium.—L. i./09,834.

Through the bite of ticks from Nyassaland, collected in the hut of a native in whose house cases had occurred, Leishmann was able to infect a monkey. The spirochetes appeared in the blood of the animal on the sixth day and it died on the thirteenth day. From the monkey, transmission had been possible to mice.—B.M.J. ii./08,1435.

**Tropical Ailments** as met with in Great Britain—malaria, hæmoglobinuria, dysentery and sprue, beri-beri, &c.—J. Cantlie, B.M.J. i./07,1465.

**GUINEA WORM, DRACUNCULUS MEDINENSIS.**—Life history of, see Leiper Rep. Advisory Comm. of the Tropical Disease Research Fund, 1906; also B.M.J. i./07,129,157.

### **Trypanosomiasis or Sleeping Sickness.**

The disease is endemic on the West Coast of Africa, notably in the Congo Basin. It is believed to be caused by the entrance into the blood and cerebro-spinal fluid of the parasite *Trypanosoma Gambiense*. It causes a complete dislocation of the brain functions, slow inflammatory process goes on in the brain cells for years, gradually the individual becomes languid in the extreme, he has not

physical energy enough to walk, speak, or even feed himself. The trypanosome of Gambia was first named and described by Dutton, who lost his life in 1905 in West Africa whilst engaged in his work on this disease. The blood or cerebro-spinal fluid of an infected person has been injected into a monkey with result that the animal died with all the symptoms of sleeping sickness. It is transmitted from the sick to the healthy by a tsetse fly (*Glossina palpalis*) and not by other biting flies (*Stomoxys*). In the stomach of this fly the trypanosome multiplies by fission. The parasite was discovered by Castellani in Uganda, but an Englishman, Dr. Adams (1901) first entertained the idea that sleeping sickness was caused by Trypanosomes. For recent work see B.M.J. ii./II, 285, 1028, 1263; L. ii./II. 459. For latest work regarding advised extermination of big game, etc. see p. 340 and 341.

Mott gives some analogies between trypanosomiasis and syphilis. Possibly the fashion in which the two organisms (*T. Gambiense* and *Sp. Pallida*) originally invaded man was the same. *T. Gambiense* can usually be found in the blood with ease, *Sp. Pallida* cannot, and seems able to multiply only in lymph spaces and channels. Possibly the deadly results of infection with *T. Gambiense* as compared with other trypanosomes is due to *T. Gambiense* having acquired the habit of migration into the subarachnoid space.

As to Organic Arsenic bodies Mott thinks possibly the trypanocidal and spirillicidal action due to their stimulating phagocytosis,—possibly to their having an affinity for the phosphorus-containing lipoids of the periplasmic membranes of the organisms in question. Toxic effects of Organic Arsenic Compounds on the other hand may be due to its union with the lecithins of the nervous system. Patients, therefore, seem to stand between the devil and the deep sea.—B.M.J. ii./10, 1647.

Spirochetes are generally believed to be linked to the protozoa rather than to bacteria. A Spirochætal invasion clinically differs from a bacterial one and conforms especially to certain trypanosome infections and there is great similarity of the histological lesions of the nerve tissues of chronic trypanosome infection,—e.g., sleeping sickness and the *mal de coit* (Dourine) of horses (transmitted by *T. Equidermum*)—to syphilitic and parasymphilitic lesions. There is further similarity in the fact that lymphocytes and plasma cells are found in the cerebro-spinal fluid in trypanosome diseases of animals and man, e.g., sleeping sickness.

*Sp. Pallida* though now transmitted direct from man to man was possibly at one time dependent upon a biting insect, just as now is the Spirochete of tick fever.

One essential difference in effects on the nervous system between *T. Gambiense* and *Sp. Pallida* is that whereas every case of this trypanosome infection leads finally to invasion of the nervous system, yet in syphilis not more than 5 or 10% even of untreated cases do this.

Trypanosomes are always found in the cerebro-spinal fluid. Spirochetes have never been demonstrated in it.

*T. Gambiense* is the special organism of sleeping sickness whether acquired in the Congo State, or any other portion of Africa. Europeans are just as easily attacked as the natives. It is very doubtful whether the Organic Arsenic Compounds, Mercury, Trypan Red, etc., though causing the trypanosomes to disappear from the blood, will attack same when once in the cerebro-spinal fluid, as these drugs do not pass from the blood into the cerebro-spinal fluid. Various workers have suggested that the trypanosome may pass into latent endocellular form.

Some experiments on clearing the natives from the shores of Victoria Nyanza were thought to prove that *Glossina Palpalis* retained its infectivity for a period of two years, but there may be numerous means of re-infection of the flies.



Full clinical Study and Pathological data of Human Trypanosomes, *vide* Mott.—P.R.S.M. Path. Sect. Nov. '10, p. 1, *et seq.*

Spirochetes are regarded as primitive or transitional forms leading up from the bacteria and their allies to the flagellates. Doflein's *Lehrbuch der Protozoenkunde* is advised as a complete study of Protozoa from the zoological standpoint.—B.M.J. i./10,142.

Involution Stages of Trypanosomes —Na. Oct. 1911 575.

Research was instituted by arguing from analogy with the Tsetse-fly disease in cattle. It was found that *Glossina palpalis* can carry the disease for a period of 48 hours from the sick to the healthy.

The *glossina* must be exterminated, but in addition immunisation experiments have been undertaken, the principle being to pass a strain of trypanosoma through different races of animals until a certain degree of virulence is lost. Laveran has made preliminary attempts by means of horse serum. A similar process was carried out by Koch with success in the allied Indian disease in horses—surra.

The condition of the stomach in sleeping sickness is a marked feature. It is comparable with the petechial hæmorrhages met with under the endo- and epicardium of the heart in other trypanosomic affections.—L. ii./05,1909.

The trypanosome was found in the spinal fluid of 70% of cases (34) of sleeping sickness—in all of which the spinal fluid was examined. Sleeping sickness presents three stages. Koch's immunising experiments.—Castellani, B.M.J. ii./04,71.

Laveran—a paper on prophylactic inoculations against trypanosomiasis, malaria, and piroplasmiasis.—L. i./06,1198.

Nabarro and Greig show sleeping sickness can be conveyed by other species than *glossina palpalis*.—B.M.J. ii./06,1881.

Meat is one of the cravings of the sufferers. Of 300,000 round the Victoria Nyanza 200,000 were swept out of existence.—'The Times,' April, 1908.

Hodges does not see any need to suppose the existence of any other means than *Glossina palpalis* of spreading the infection amongst human beings.—Sleeping Sickness Bureau, London, L. i./09,483.

Examination of infected villages showed that '*palpalis*' villages are more heavily infected than the '*morsitans*.'—B.M.J. i./09,403.

Serum Therapy suggested,—i.e., the injection of a highly immune serum—obtained from the blood of patients recently recovered,—or rather, as these are few and far between, of patients subjected in the first instance to chemotherapy (Atoxyl, &c.).—L. i./09,716. The injection to be intra-spinal—the serum could be taken from a patient improving. The blood of those suffering from trypanosomiasis contains trypanocidal bodies—the intra-spinal treatment could be combined with chemical treatment through the blood.—B.M.J. i./09,1176.

Liquor Arsenicalis as routine suggested treatment.—B.M.J. i./09,681.

If a fly, three weeks after feeding on an animal suffering from sleeping sickness, were incapable of giving infection, trypanosomes were not found in its stomach. Further trypanosomes were not found in flies which had been kept from infection, nor in flies fed on healthy monkeys.—B.M.J. ii./09 903.

Potassium Chlorate 0.03 Gm. in  $\frac{1}{2}$  Cc. of 1 in 10,000 Saponin Solution efficacious in prolonging life of guinea pig infected with trypanosome. Similarly 1 mgr. of Arsenious Acid in  $\frac{1}{2}$  Cc. of 5% Anilin Chloride Solution. By the last mentioned, trypanosomes were made to disappear permanently, but not stated to be a definite cure.—B.M.J.E. ii./09,56.

Observations on various spirochetes show that they divide both longitudinally and transversely, usually one after the other, but may occur simultaneously.—B.M.J. ii./09,1244.

Bagshawe on advances made during 12 months prior to Oct. '09, in prevention and cure of sleeping sickness. Kleine showed that it takes about 20 days in the case of *T. brucei* after the fly has ingested the trypanosome before it is capable of infecting susceptible animals. Bruce confirmed this for *T. Gambiense*. Some flies probably remain infective for the rest of their lives. Bruce introduced fluid swarming with trypanosomes from the gut of a fly, fed 75 days before on an animal infected with *T. Gambiense* and subsequently on healthy animals,—into a monkey. After 8 days the monkey became infected. This indicates some form of development, whether a sexual process or merely multiplication as seen in cultures is not known. Sleeping sickness does not become endemic except in districts in which *glossina palpalis* is in evidence. That

this fly is a transmitter of human trypanosomiasis has been known since 1903. Sexual coitus has been thought by Koch and Kudicke to explain the occurrence of the disease in *palpalis*-free areas. The suggestion that other "auxiliary" flies are responsible in addition is refuted. Diagnosis by direct examination of the blood gave a large percentage of successes, particularly on centrifugalising as also the examination of the glands, cervical and submaxillary, in particular. Gland palpation is employed in preliminary diagnosis. A single dose of Atoxyl will cause marked retrogression in the size of infected glands—the larger the glands the more likely the existence of trypanosomes within. In the matter of symptoms it would appear that paralysis, paresis, and epileptiform convulsions, which among untreated cases, occurred in small percentage, are now commonly met with, and are often followed by sudden death, which was very exceptional before the use of Organic Arsenic.

*Sudden or rapid death was frequently the termination of cases of sleeping sickness treated with full courses of Organic Arsenic.*

There are indications that nature is working out a cure for herself by attenuating the virulence of the trypanosome, or by some other factor or combined factors.—L. ii./09, 1193; B.M.J. ii./09, 767; see also Jl. Trop. Med., Nov. 15 1909.

The following notes are taken from the "Report on Measures adopted for the suppression of Sleeping Sickness in Uganda, by Sir H. Hesketh Bell, K.C.M.G., being Parliamentary Colonial Report, No. 63 Uganda.

The disease appears to have come from the Congo basin. At Kampala in 1901 eight cases of a mysterious disease were first noted.

The total mortality in the Uganda Protectorate from the scourge up to end of 1906 considerably exceeded 200,000. A number of investigators were sent out by the Royal Society. Koch, who arrived in 1906, devoted himself to curative methods, using Atoxyl in particular in large and repeated doses. The method seems hopeful, but in view of the protracted duration of the disease, and variety of the phases, some years would have to elapse before any cure could be considered permanent. The disease so far appears to be incurable. The best recommendation seems to have been to remove the entire population to fly-free areas. Citronella plantations are in a flourishing condition, and probably drive away several kinds of noxious insects, but they have been disappointing (p. 44). The segregation camps justified existence in several particulars. Drugs have prolonged lives, but not a single undoubted cure among thousands of cases that have passed through the camps.

In February, 1909, Kleine stated that the trypanosome must pass through a cycle in the fly of at least 17 days, and until this had happened it was unable to transmit the disease. He proved flies capable of conveying infection up to the 75th day. Bruce later found *Glossina palpalis* capable of retaining infectivity for two years.

Deaths during 1909 only 459, as against 5,000 in 1907. Vide Na. May 5 1910, p. 280, also E. M. Holmes, P.J. ii./10, 734, for *résumés*.

B.M.A. DISCUSSION ON TRYPANOSOMIASIS.—There is no absolute proof that a single person has recovered from sleeping sickness. There were some 49 cases among Europeans between 1908 and 1910,—in Europeans chance of recovery is greater than in natives. It is difficult to understand how the flies retained infectivity for two years after the native population had been removed from the shores of the Victoria Nyanza. Possible explanations are given. Experimental injections into Hippopotami, etc., negative so far. With regard to epidemiology, possibly a considerable degree of saturation with *Glossina* is necessary before an epidemic spread of sleeping sickness takes place. With regard to possibility of hereditary transmission of *T. gambiense*, *T. brucei*, etc., by the respective infected *Glossina* to their progeny the majority of experiments so far conducted were negative, but L. W. Sambon still holds this view.—B.M.J. ii./10, 864, *et seq.*

**Eighteenth Bulletin of the Sleeping Sickness Bureau.**—It is suggested that *Glossina Morsitans* is harmless to man when occurring on open and relatively high ground, and probably dangerous in the presence of a sleeping sickness "reservoir" when inhabiting damp and warm valleys. Possibly the development of the trypanosome in the body of *Glossina*, which in favourable circumstances is only in about 5% of these flies, does not occur in relative cold or dryness.—L. ii./10, 323.



In the 20th Bulletin of the S.S. Bureau records of 50 cases of Europeans are given,—of these thirty are known to be dead. One of the survivors, infected probably in 1900, is regarded as cured with Fowler's Solution.—Na. Oct. 13/10, 469. For recent deaths, *vide* p. 341.

The staying of the disease in Uganda by clearing the Northern shores of Victoria Nyanza of its human inhabitants can only be temporary. The measure is not curative. It will be necessary to determine whether the animals in the district are capable of acting as hosts of the parasite.—B.M.J. i./11, 82.

The domestic fowl is not a reservoir for *T. Gambiense*, but the antelope is possibly. Results of a large number of experiments were negative in every case with fowls.—B.M.J. i./11, 253.

Experiments on eleven antelopes showed that after tsetse flies had been fed upon them, their blood eight days later transmitted the disease to all the monkeys inoculated, while two-thirds were infected after an interval of thirty days. The antelopes remained in perfect health, although in eight of them trypanosomes appeared in the blood for a few days only. No wild antelope inhabiting the Victoria Nyanza shore has yet been found to be naturally infected. Birds cannot act as a reservoir of the trypanosome.—Sir D. Bruce, Roy. Soc's. Commission Report, Jan. 1911.

**Cold Chamber Treatment.**—Results with animals inoculated with *T. gambiense* and *T. rhodesiense* showed advantage of the treatment. The chamber can be kept at any temperature between 15° F. (9.4° C.) and 150° F. (65.5° C.) The cold is produced by an Ammonia Compressor and a fan which drives in air through a chamber in which Saturated Solution of Calcium Chloride is kept constantly trickling over corrugated iron plates. A sleeping sickness patient underwent the treatment and felt better for it.—B.M.J. i./11, 678.

*Trypanosoma lewisi*,—the common rat trypanosome, is akin to the Trypanosome of sleeping sickness. The mechanism of infection is the act of *eating* infective fleas and not by being bitten or contaminated by them. C. Strickland.—B.M.J. i./11, 1049.

Contrary to Strickland (B.M.J. i./11, 1049) E. A. Minchin and J. P. Thomson bring evidence that infection of rats with *T. lewisi* is not in general normally effected through the rat eating fleas,—they believe that the ripe infective form of the trypanosome,—the final form of life cycle which it passes through in the flea,—is regurgitated from the stomach of the flea into the wound made by the proboscis during the act of feeding.—B.M.J. i./11, 1309.

*T. evansi* causes the disease surra in elephants, camels, horses, etc., in India and Africa. The carrier of surra has not yet been identified. There are no tsetse flies in India. Details of differences between *T. evansi* and *T. brucei* are given.—Sir D. Bruce, Roy. Soc. per Na. June 15, 1911, p. 539.

*T. rhodesiense*, the agent in a case of sleeping sickness.—Na. June 15, 1911, p. 539.

See also *Organic Antimony and Arsenic Compounds* (Vol. I.) for recent treatment and refs.

**Trypanosoma Gambiense, Characters of.**—Morphologically, a long-shaped protozoon containing a large nucleus centrally and a vacuole or contractile vessel at the larger end.

The single flagellum proceeds from a small mass of chromatin at the anterior end. This flagellum forms the edge of undulating membrane which is observable from end to end of the organism, and continues in the same direction for some length as a free tail. It measures 18 to 26  $\mu$  by 1.4 to 2  $\mu$ .

Analogy has been drawn with certain other flagellates—notably trichomonas, englena and herpetomonas. Trichomonas move both backwards and forwards, Englena and Herpetomonas move only forwards, and the trypanosoma backwards—by the aid of the membrane. At the spot slightly behind the vacuole there are some patches of pigment—the so-called eye spots, centrosome or micronucleus.

Trypanosoma reproduces itself by longitudinal division or fission—in addition there is sometimes transverse fission—and formation of rosettes by multiple division. Before the fission there is a division of the centrosome, followed by division of the flagellum, nucleus and the protoplasm—these dividing forms are not easy to find in the blood.

The organism may be found in large numbers in the blood in every case of sleeping sickness, as also in the lymphatic glands and in the advanced disease in the cerebro-spinal fluid.

There is no great reduction in the number of red corpuscles. The hæmoglobin is also not decreased.—L. i./o6,227.

Staining is best conducted with Leishman's Stain *q.v.*; some beautiful specimens can be made with this by first pouring on to the film and allowing to stain half a minute, then add twice the volume of distilled water and allow to stain further half an hour. Wash in distilled water and dry in customary manner.

Other methods of staining are with Thionin Blue, Methylene Blue, and Borrel's Blue, *q.v.*

Manson recommends the examination of the blood when the temperature is high: it is well to centrifugalise as the trypanosomes accumulate in the leucocyte layer above the red corpuscles.

Classification of some trypanosomes:—*T. Evansi* (discovered 1880), causing "surra" in India. *T. Elmastiana* (1901), causing mal de caderas in South America. *T. Brucei*, found in cases of tsetse fly disease or nagana, in Zululand, Bruce, 1894. *T. Rougeti* (1896), the parasite of dourine or mal du coit, occurring in South Europe, North Africa, and other parts. *T. Lewisi*, non-pathogenic, found in rats. On injecting into other animals is removed by phagocytosis. *T. Neveu* (1890), found in man in Algeria. *T. Castellani* (November, 1902) found in Uganda by Castellani, occurs in the cerebro-spinal fluid in cases of sleeping sickness. It is closely allied to *T. Gambiense*. The tsetse fly, *Glossina palpalis*, is common in the Upper Congo and Uganda; *Glossina morsitans*, as shown by Bruce in 1894, being responsible for nagana, or tsetse fly disease in animals.

Trypanosoma has been cultivated in the condensed moisture which arises from a blood agar medium.

Manson in a lecture on advances of science upheld the view of a sexual reproduction of the Trypanosome in its insect vector.—L. ii./o8,991.

#### Laveran's Method of Staining Trypanosoma.

Prepare thin blood films, and fix in absolute alcohol 5 to 10 minutes. The following are required:—

- (1) *Solution*.—Methylene Blue and Silver Oxide (Borrel's Blue). Prepare "some" Silver Oxide freshly by means of Silver Nitrate and Sodium Hydroxide. Wash the precipitate with distilled water thoroughly, and add to it a saturated solution of medicinal Methylene Blue. Allow to remain for a fortnight, occasionally shaking.
- (2) Aqueous Solution of Eosin 1 per 1,000.
- (3) Solution of Tannin 5%, or, better, a solution of 'Tannin Orange'.

Mix just before use: No. 1 Solution 1 Cc., No. 2 Solution 4 Cc., Distilled Water 6 Cc.

Stain in a flat dish, film downwards, for 5 to 20 minutes—5 to 10 minutes is enough in most cases. Wash in water and treat with tannin for a few minutes. Wash in water and then in distilled water. If precipitate found on the preparation wash in Clove Oil and brush off with Xylol.

Secretary for the Colonies on prevention of trypanosomiasis.—An interesting account. Instead of wiping out the wild animals which may be source of infection, it is advised to destroy *G. Morsitans*, by cultivating the soil. Heroic measures founded on half knowledge are a mischievous form of human folly.—B.M.J. ii./12,41.

Work by the Royal Commission (*c.f. antea*) in the Luangwa Valley, Northern Rhodesia has demonstrated that this district is free from *Glossina palpalis* but is infested with *Glossina Morsitans*. This fly is the carrier of *T. Rhodesiense* which is distinguished from *Tr. Gambiense* by the posterior displacement of the macro-nucleus. Approximately 5 per cent of these flies may become permanently infected and capable of transmitting *T. Rhodesiense* to monkeys and other mammals and presumably to man. The period between the infecting feed and when they become infected is approximately 14 days (minimum duration of cycle in *Gl. palpalis* is 18 days). Certain animals, namely, waterbuck, mpala, hartebeest and warthog



were found to harbour a trypanosome indistinguishable from *Tr. Rhodesiense*.

*Schizotrypanum cruzi* is a trypanosome-like body which in Brazil causes a disease quite different in its symptoms from the African sleeping sickness and trypanosomiasis. The symptoms seem to be particularly those of thyroid and supra-renal insufficiency. Fever is present and the lymphatic glands, spleen, liver and thyroids may be enlarged. The parasite is not unlike the *Leishmania* body.—Review of Tropical Diseases, Pr., Aug. '12, 261.

Sleeping sickness in Rhodesia, Nyasaland and adjoining territories is due to *T. Rhodesiense*,—not to *T. Gambiense* recently introduced there.—B.M.J. ii./12, 201.

Doubt as to whether the trypanosome found in big game is the same as that known in man as *T. Rhodesiense*. Experiments suggested.—B.M.J. ii./13, 150.

Big game, especially antelopes, are the reservoirs of, and *G. Morsitans* is the cause of trypanosomes fatal to men and animals.—A letter in support of extermination.—B.M.J. ii./13, 207.

Colonial Office Committee nominated to report on game destruction or other measure to control the disease, *ibid*, 262.

Nyasaland Sleeping Sickness Diary. Deaths during first four months of 1913 totalled 128,—*ibid*, 349. The next eight months accounted for 25 deaths,—*ibid*, 1652.

*T. Gambiense* and *T. Rhodesiense* not specific to human beings. They can live in various species of antelopes without producing disease in them. Domestic stock also harbour these Trypanosomes. Experiments suggested,—*ibid*, 756.

Identity of *T. Rhodesiense* with Trypanosomes found in game.—B.M.J., i./14, 1234.

Blood containing traps suggested for catching flies, as used on the Nile for catching insect pests.—A. Balfour, B.M.J. ii./12, 11.

For further references to trypanosomiasis, v. Vol. I. p. 139—142, 165 et seq.

## **Bacillus Tuberculosis.**

### **Relationship between Human and other forms of Tuberculosis.**

The late R. Koch denied that bovine is identical with human tuberculosis, and believed that cow's milk and meat cannot give rise to human tuberculosis.—c.f. B.M.J. ii./01, 190; L. ii./01, 187; L. ii./03, 333. V. Behring demonstrated a very close relationship between them.—B.M.J. i./03, 806. Koch's work and theory disproved: the organism is the same in both—Römer, Marburg.—L. i./05, 658.

The bacilli in man and cattle may be different varieties of the same species. Discussion.—L. ii./03, 333, 352, 399, 473, 560, 744, 788. Human tuberculosis is more generally the result of man to man infection.—L. ii./03, 850.

The Royal Commission on Human and Bovine Tuberculosis appointed in 1901,—shortly after the late R. Koch's dictum that bovine tuberculosis is not a real source of danger to man,—has concluded its labours in the form of a **final Report** (1911). The

first Report (1904); the second Interim Report (1907) and the third Interim Report (1909) are summarised (in Edn. XIV., p. 796).

The final Report finds that the human and bovine types are *morphologically indistinguishable*, but cultural characters of the organisms differ, also the pathogenic effects on different animals. The human types grow more luxuriantly, although Bovine Bacilli vary among themselves in luxuriance of growth. *Re* pathogeny, the bovine is pathogenic to cattle, rabbits, goats, chimpanzees, monkeys and pigs, while the human is fatal to guinea-pigs, chimpanzees and monkeys, but causes only slight and non-progressive lesions in cattle, goats and pigs. Possibility of transmuting one type into the other cannot be denied, though experiments for the most part failed. Both types have been obtained in certain instances from the same patient. *The cultural differences are, however, not sufficient to establish the two as distinct organisms. In a considerable proportion of cases of tuberculous disease in man the lesions are caused by bacilli in every respect indistinguishable from the bovine type.*

*Mammals and man can be reciprocally infected.* Bovine animals are not completely immune to the human type, although they possess a high degree of resistance to it. The bovine has been found in man. The majority of human cases from which bovine bacilli were recovered were instances of tuberculous disease in children. *Infection by cow's milk, beef and pork is possible,—infants and young children are, therefore, specially endangered.* Even in adolescents and adults so large a proportion as 5 out of 55,—the number investigated—showed the presence of the bovine type as to indicate the same source of infection as are possible at other periods of life.—B.M.J. ii./II,122. Government should legislate especially regarding meat and milk production.—L. ii./II,166.

The fact is proved beyond question that tuberculous affection of the cervical glands and of the peritoneum in young children is in a large number of cases set up by the bovine type. With regard to infectivity of milk the importance of dosage in the transmission of tuberculosis is brought out. The virulence of the subsequent infection is almost always in direct proportion to the size of the dose administered,—this doubtless accounts for the diminishing susceptibility of the human subject to the effects of the bovine type of disease as age advances.—B.M.J. ii./II,180 (Leader). *Vide* also B.M.J. ii./II,628,634.—Review of the first volume of the **Appendix to the Final Report.**—see also P.J. ii./II,492.

Royal Commission on Tuberculosis—2nd Vol. of **Appendix** to final report reviewed.—B.M.J. i./12,78. 3rd Volume of **Appendix** reviewed *ibid*, p. 436.

Prof. Gosio, of Italy, endeavoured to upset the findings of the Royal Commission on Tuberculosis. He claims that where there is much tuberculosis in animals there is little in man and *per contra*, where there is much in man there is little or none in animals. Data are brought forward showing that consumption of European cows' milk is associated with prevalence of tuberculosis in various countries, whilst, *e.g.*, in Morocco, where there are no European dairy cows, tuberculosis is unknown.—B.M.J. i./13,96.



**Possible Test to distinguish Human and Bovine Types of Tubercle Bacillus.**—The rabbit (synovial membrane of the knee joint) is injected with a bacillary emulsion (not mixed infection) or with pus or other pathogenic fluid. By the amount of reaction it is claimed possible to determine nature of infection, *i.e.*, if bovine the changes are rapid and acute, if human the reaction is only slight. The distinction is stated to be clinically and pathologically most striking.—B.M.J. ii./12,1433.

A report on the results of a chemical investigation undertaken by Arthur Harden, F.R.S. (assisted by S. G. Walpole), at the request of the Royal Commission has been published as Appendix, Vol. VI., of the final Report of the Commission. It contains a systematic quantitative comparison of the action of the two types, and shows that **no definite physiological difference** has been detected between the human and bovine types of tubercle bacilli. The report contains much bacteriological and chemical detail, and must be consulted by those requiring detail of the investigation.

**INTERNATIONAL CONGRESS AT WASHINGTON.**—Bacilli of the bovine type have been found in the cervical lymph glands of man, and in relation to the human intestinal tract, but with few exceptions these bacilli are but slightly virulent for man and remain localised. The crusade must be against the 'human' type.—Koch. Koch had lost his battle. He stood alone in the field.—B.M.J. ii./08,1190,1201.

Pulmonary tuberculosis is in immense majority of cases probably not contracted by inhalation but the germs enter through the intestinal tract. Future research will explain how in China, where the consumption of the milk of bovines is practically *nil*, tuberculosis is everywhere prevalent amongst the natives.—Whitla, B.M.J. ii./08,68.

Results of tuberculin test on cattle compared with a number of cases of tuberculosis in people employed on the farm in question. Conclusion was that tuberculosis in man and that in cattle have a certain relation to each other. Reaction in cattle on farms where human tuberculosis has been traceable occurs nearly three times as frequently as in farms where this disease was not found.—L. ii./08,362.

Review of difference between Human and Bovine.—Bonney.—B.M.J. i./09,669: *vide* also B.M.J.E. i./09,12,100.

**INTERNATIONAL TUBERCULOSIS CONGRESS AT ROME.**—B.M.J. i./12,903,950.

Infection of the human being by the tuberculous cow can and does occur. An answer to "Dangers of Sterilised Milk," by R. Mond.—L. i./14,145.

Portals of entry of the Tubercle Bacillus include, especially in childhood, the respiratory system, alimentary tract, mucous membrane of the nasopharynx, the skin and the placenta—antenatal infection. Necessity of directing prophylaxis towards suppression of contamination from man to man and principally in the family. Bovine infection is of less frequency.—E. Emrys-Roberts, B.M.J. i./13,210.

Tuberculous Milk in Edinburgh, Report on, 20% of samples examined were tuberculous.—B.M.J. ii./14,71.

**Tuberculosis in Dogs** is comparatively rare—it is almost invariably due to infection from a human source. The symptoms—emaciation, loss of strength, etc., are easily recognised.—B.M.J. ii./13,827. On the other hand we read the prevalent opinion that dogs are practically immune to tuberculosis is erroneous. In three years 165 cases were recorded, all being verified anatomically and bacteriologically. The disease is more prevalent among dogs in town than in country districts. Cats also are capable of infection but are less frequently affected than dogs. Horses seem to be very rarely affected, scarcely one, in 15,000 cases examined, has been recorded.—Cadiot, P.J. i./14,287.

Persons of gouty 'diathesis' or of gouty parentage show a marked resistance to tubercle.—H. E. Waller, Pres., Nov., 1913,298.

From a study of the subject in Manchester not less than 25% of the tuberculous children under five years of age suffered from infection of bovine origin and this estimate is much lower than one based on probabilities would be.—Prof. S. Delépine, B.M.J. ii./12,1486.

Hamburger came to the conclusion that 95% of all the children in Vienna, aged 15 are infected with tuberculosis, the infection being by aspiration from man to man.

Tuberculosis in infancy. An investigation into the conditions in Edinburgh (371 cases) compared with results of Hamburger and others. Bovine

infection in the Edinburgh cases have a considerable share in tubercle infection in that city.—B.M.J. ii./12,677.

In England and Wales in 1909, 10,000 children under the age of 5 died from tuberculosis (other than pulmonary tuberculosis) and it is estimated that 70% of our dairy cattle are affected with tuberculosis.—B.M.J. i./13,96.

**Ziehl-Neelsen method** ; Sputum and sections.—1. Prepare film from sputum or a section ready for staining, and fix by usual methods. 2. Boil filtered carbol-fuchsin in a test-tube and cover specimens with it entirely ; stain films 5 mins., sections 10 mins. (**Carbol-Fuchsin Solution**, Neelsen's Solution, is prepared by mixing Concentrated Alcoholic Fuchsin Solution 1 with 5% Carbolic Acid Solution 9, slightly warmed.) 3. Wash well in water. 4. Decolourise almost completely by immersing in 25% sulphuric acid. 5. Wash well in water. 6. Counter-stain with **Alkaline Methylene Blue**—sputum, 1 to 2 mins. ; sections, 3 to 4 mins. This stain is prepared by mixing saturated Alcoholic Methylene Blue Solution 142 mins., with 1 ounce of a 1 in 10,000 solution of Caustic Potash. (Note.—Medicinal. Methylene Blue is far more soluble than ordinary and should be used.—W. H. M.) **Carbolised Methylene Blue** is also employed :—Dissolve Methylene Blue 1 as much as possible in Alcohol 90% 7, and add Phenol Solution 5% 70 allow to settle and decant. 7. Wash, dry, and mount in Xylol Balsam (sputum). 8. If section dehydrate with alcohol, clarify with xylol, and mount in xylol balsam. If dehydrated with anilin oil instead of alcohol a clearer preparation is produced.

Examine wherever possible the first sputum expectorated after the night's sleep.—L. ii./10,1747.

**Fuchsin-Anilin Green Method** for staining *B. tuberculosis*.

Solution A. Fuchsin 10, Absolute Alcohol 100.

„ B. Strong Ammonia Solution 3, Water 100.

„ C. Water 80, Nitric Acid 20, Malachite or Iodine or Acid Green q.s. to saturate. Methyl Green does not give satisfactory results.

Add one part of A to 10 of B. Warm until vapour arises, immerse 1 minute, wash with water, then immerse in C 40 seconds. Wash off thoroughly. Bacilli red on pale green ground.

**RECOGNITION**.—Delicate, straight, or more usually slightly curved rods. When stained, usually beaded in appearance. The length of the organism is commonly said to be about one-quarter to one-half the diameter of a red blood-corpuscle, but it varies considerably. Involution and branching forms occasionally met with. (Gram +).

The Tubercle Bacillus is about  $1\ \mu$  in length when grown on Blood Serum and from 1.25 to  $6.5\ \mu$  in the tissues.—Hewlett, B.M.J. i./12,75.

Present in large numbers when the process is acute, but are relatively scanty or absent in chronic forms of tuberculosis, *e.g.*, Caseous non-suppurating glands lupus, &c

Tubercle Bacilli contained in sputum retain their vitality for a considerable time, even when the sputum dries up.

**Rosolic Acid Method**.—Specially for *B. Tuberculosis* in tissues. Stain in hot carbol fuchsin for 5 minutes. Wash quickly in tap water. Dip five or six times in saturated Alcoholic Solution of Rosolic Acid (Corallin) till fuchsin is removed. Wash in water and counter-stain in saturated Alcoholic Solution of Methylene Blue.

**Cultural Characters**. *B. tuberculosis* was first grown on blood serum by Koch, but will not grow without addition of glycerin to the ordinary media. Requires temperature of  $37^{\circ}\text{C}$ . Dry wrinkled growth somewhat like a lichen, on glycerin agar in three weeks. Cultures, especially in glycerinated broth, have fruity odour.

To obtain a pure culture of the organism from tubercular material it is necessary to inoculate guinea-pigs with same, and after a lapse of four to six weeks cultures are made from enlarged glands direct on to blood serum or glycerin potato. Glycerin agar is not recommended for use direct *post mortem*, but the organism flourishes on this on sub-culture.

**To exclude Acid-fast Bacilli and all other Bacteria except Tubercle and Leprosy.**

1. Wash film in Alcohol after fixing by radiant heat.
2. Stain with hot Carbol Fuchsin.
3. Differentiate in 25% Sulphuric Acid and wash freely in tap water and Alcohol.



4. Counterstain in Picric Acid and Alcoholic Solution. Dry and examine by 1/12th inch immersion lens.—Wyatt Wingrave.

**POINTS OF DIFFERENCE BETWEEN HUMAN & BOVINE TUBERCLE BACILLI.**

*Human.*

*Longer and slender.*

*Fasciculated.*

*Colour true.*

*Beading well marked and regular.*

*Bovine.*

*Shorter, thicker, stumpy.*

*Discrete, not in bundles.*

*Not colour true, receptive of blue.*

*Beading less marked.*

—Wyatt Wingrave.

The "**Picric**" Method (for the staining of both types of bacilli) Picric Acid is used as a mordant for the Fuchsin, in addition to the Phenol. Twin films are used for comparison, one being taken for the "Ziehl-Neelsen" method, and the other for the "Picric." Stain with Carbol-Fuchsin with gentle heating. Pour off Fuchsin, and add Alcoholic Solution of Picric Acid until film is yellow, wash and dry. (Found delicate.)—L. ii./10,1752.)

**Hermann's Crystal Violet Method and Much's Modified Gram Method** of staining *B. Tuberculosis* are described in the B.M.J. ii./12,412. The former has some disadvantage in technique. Much's method is not suitable for direct investigation of sputum.

*The British Royal Commission on Tuberculosis found it impossible to differentiate between the human and bovine types of tubercle bacilli by means of staining methods.*—Pr. Mar. 1911, p. 420.

**ANTIFORMIN** (Patented in 1900) contains about 7.5% free Sodium Hydrate and 5.3% available Chlorine. Another statement is to the effect that its composition is equal parts of Eau de Javelle (Liquor Sodæ Chlorinatæ) and 15% Solution of Sodium Hydrate. A disinfectant. In 2 to 5% dilution kills most bacteria in 5 minutes. Anthrax Spores, require 10% for 12 hours. It does not, however, kill Tubercle bacilli (probably by reason of the fatty envelope which is believed to enclose them). It can be used to isolate the bacillus from the sputum—particles can be removed by macerating 2 hours 20 to 30 Cc. of tuberculous sputum with 15 Cc. of the Antiformin and diluting with water to 100 Cc. These inseminated on blood serum are stated to produce a pure culture.—M. 08,130. B.M.J.E. ii./08,56; ii./09,8—or may be used for staining direct, *vide infra*.

It dissolves hair, wool, silk, etc., also 0.5% is stated to dissolve Cholera Vibrios, Spirochetes, Trypanosomes in 5 minutes, while a 2.5 to 5% solution completely destroys vegetative forms of bacteria.

**Uhlenhuth's Antiformin Method of isolating B. Tuberculosis**—(modified by Koslow). Shake the Sputum with Antiformin in a glass stoppered cylinder, the amount of Antiformin varying with the consistence of the sputum,—if very viscid or dense, an equal volume, if thin, half the amount may suffice, occasionally during five minutes, then dilute with Distilled water approximately 10 times the amount if Antiformin used,—again shake a few minutes. Finally add a mixture of equal parts of Ether and Acetone, equal in volume to that of the water. Shake a few seconds and allow to stand. Three layers will form. The middle one,—a more or less white ring, will contain nearly all the Tubercle Bacilli present in the sputum. Draw off with aid of a pipette and test. This may be centrifugal sed but it is not necessary. Before staining it is well to wash film in 5% Sulphuric Acid to neutralise adhering alkali, then wash to remove acid. This method of search for Tubercle Bacilli is most thorough and certain.—B.M.J. ii./11,596; see also B.M.J.E. i./11,80.

**Loeffler's Modified Antiformin Method.**—To 5 to 20 Cc. of sputum add equal volume of Antiformin 50% diluted with water. Heat until clear liquid results. To 10 Cc. of the mixture add 10% Solution of Chloroform in Alcohol (5 Cc. generally suffices). After shaking centrifugalise 15 minutes. An opaque layer is then formed between the Chloroform which occupies the bottom of the centrifuge and the supernatant fluid. Pipette off the latter and remove the opaque layer wholly on to a slide. Make films fix and stain. This method is said to be rapid and simple and to give good results.—L. ii./11,1747.

As used at the Lister Institute the sputum is mixed with an equal quantity of a 30% dilution of Antiformin, and the mixture incubated over-night at 37° C. After centrifugalising the fluid is poured off and replaced by an equal bulk of Normal Saline. After shaking up, again centrifugalise. Films from the deposit thus washed adhere better to the slide. Its use is justified by small percentage of 'corrections.'—B.M.J. ii./12,411.

Cruikshank employs Antiformin for isolation of the bacillus, then inoculating Glycerinated Egg Medium with centrifugalised sediment. The Bovine Bacillus grows best *without* Glycerin.—B.M.J. ii. 12,1298. Emery, Pr. Feb. 1910, p. 467.

**Detection of Tuberculosis in fæces** by aid of Antiformin. Until recently it was thought that the discovery of *B. tuberculosis* in fæces was diagnostic of tuberculous enteritis, —the bacillus, however, frequently occurs in fæces of patients suffering from pulmonary tuberculosis.

Acid-fast bacteria resist Antiformin when diluted to 20% for 2 to 5 hours—other bacteria and organic matter generally are speedily dissolved. A small piece of fæces (about a cubic  $\frac{1}{4}$  inch in size) is placed in a conical glass and to this some 20 Cc. of Antiformin diluted with Water to 15% is added and the whole well mixed. More of the diluted Antiformin is added and the mixture allowed to stand for about an hour. A white curdy precipitate appears on mixing and settles. Beneath this white layer some unchanged fæcal matter remains and above the white layer the fluid is of a clear yellow or brownish color. A drop or two from the white curdy layer is mixed with a drop of Albumin Water and stained by the Ziehl Neelsen method. Much searching may be necessary. For certainty Alcohol may be used in addition to Acid for decolorising.—B.M.J. ii./10,184; L. ii./10,1747. See also B.M.J.E. i./10,36.

A granular form of *B. tuberculosis* exists which does not stain by Zeihl-Neelsen method. Much's modified Gram method described.—B.M.J.E. ii./09,44

### Albumin Reaction in Tuberculosis.

The reaction is conducted as follows:—5 Cc. of Sputum are mixed with 20 Cc. of Normal Saline in a test tube. 5 or 6 drops of Acetic Acid are added and the whole shaken up and filtered. The filtrate is then tested for albumin by heat or nitric acid, using the boiling test in preference. It is said to be more useful than microscopic examination for diagnosis of tuberculous disease of the lung, even in early stages when it may be difficult or impossible to find the bacilli in the sputum. A reaction for Albumin is not constantly given in miliary tuberculosis nor in pleurisy. It is present in acute lobar pneumonia due to pneumococci during the attack, also in acute pulmonary oedema, acute congestion and acute broncho-pneumonia. As a rule it is negative in chronic bronchitis and in emphysema. In cardio-renal cases it is often positive. The intensity of the reaction in phthisis is in direct proportion to the importance and gravity of the lesions and abundance of tubercle bacilli.—L. ii./11,1084 (Clinical results with the test), 1660 (no great diagnostic value).—L. ii./11,1802.

It is a good plan to shake up the sputum with about three volumes of water, filter, centrifugalise the filtrate and stain the sediment carefully picked up with a fine pipette. Bacilli slip through the filter paper leaving cells and debris behind, and are then more easily found. Further conduct the *Albumin Test* on the filtrate, first removing Mucin with a few drops of Glacial Acetic Acid and adding a little salt solution and again filtering. W. E. Home states he has not found Tubercle Bacilli in a non-albuminous urine.—L. i./13,1828.

Practically all cases of active pulmonary tuberculosis, it is said, contain albumin in the sputum. Significance and causation 98.9% of specimens containing Tubercle Bacilli also contain Albumin.—L. ii./13,382.578.

Of prognostic value, but not conclusive.—Fishberg, quoted by W. D'Este Emery, Pr. Feb. 1913.

**Urine**—At least six films should be prepared. The specimen is centrifugalised, the supernatant liquor is poured off, and the sediment is washed two or three times by shaking up with sterile water, centrifugalising on each occasion, fix film with alcohol. Stain as for sputum, by Picric Acid method. Smegma B. is acid-but not acid-and alcohol-fast. Always wash film with albumen water before staining.

Russ has endeavoured to detect tubercle bacilli in urine, milk, &c., by aid of an electrical current. The movement of the organisms in an emulsion toward one of the poles is possibly due to chemical affinity, or to their being driven mechanically by the ions. To detect the bacilli in pathological fluid by means of a current it is necessary to add to the fluid an electrolyte in which the organisms are known to migrate. Of a number of substances tried Ethylamine was found to be best for the purpose. This produced a fair accumulative



of bacilli at the kathode. The aggregation is probably due to an affinity between the products of electrolysis and the bacteria. The method has great detective capacity. Various bacteria behave differently, suggesting the possible use of the method for diagnosis.—L. ii./09, 2; B.M.J. ii./09, 81.

The routine examination of urine of all patients suffering from albuminuria irrespective of whether blood or pus is present, will reveal presence of tubercle in a surprisingly large number of totally unsuspected cases.—B.M.J. ii./09, 997.

Tuberculous disease of the kidney too often goes unrecognised until a comparatively late period.

**Ligroin method of Detection.**—To 5 Cc. of Sputum in a flask add 50 Cc. Caustic Potash Solution 5%. Shake and leave at room temperature until the sputum is homogenised. Dilute with 50 Cc. tap water and shake again. Add 2 Cc. Ligroin and shake until emulsion is formed. Warm to 60° C. until evidence of layer of smaller bubbles on the surface. A number of drops are then taken from immediately below this superficial layer and with a loop and placed on a warm slide. The dry film is then fixed with Saturated Sublimite Solution and stained by Ziehl-Neelsen method —L. ii./10, 1747. The Ligroin causes the Tubercle Bacilli to rise to the surface of the meeting of the two liquids.

**Ericolin Separation of B. Tuberculosis.**—The difficulty of contamination with other organisms, encountered when making cultures of the Tubercle Bacillus directly from a patient's sputum has been overcome by Twort, who uses the glucoside 'Ericolin' in a 2% aqueous solution. This it is said, gets rid of the other organisms. He places the piece of sputum in the Solution for about an hour at 38° C., inoculates suitable media and so obtains a growth almost, or quite free from contamination in 14 to 28 days.—Brit. Jl. of Tuberculosis, Vol. IV. (April, 1910), p. 113.

Ericolin is stated to be a constituent of *Erica Vulgaris*. Linn. Syn. *Calluna Vulgaris*, **Heather**, with formula  $C_{34}H_{56}O_{21}$ (?).

In some experiments by us to produce a glucoside from the plant, both Aqueous and Alcoholic Extractives were made and precipitated with Neutral Lead Acetate. The Liquor was freed in each case from Lead by Sodium Sulphate and then evaporated. The Aqueous Method yielded a small quantity of brownish extractive. The Alcoholic Method was carried further as follows. Concentrated to small bulk and precipitated with water—greenish resinoid 'Ericolin' obtained in appreciable quantity.

**Blood.**—The organism it is stated can be demonstrated in the blood of tuberculous patients by shaking, say 5 Cc. removed from a vein, with equal quantity of Normal Saline with 2% Sodium Citrate. Place in refrigerator 24 hours. Remove sediment with pipette and dry on slide with moderate heat. Place slide in distilled water until the blood is completely laked. Fix films and stain. The organism has been demonstrated in all of 125 cases of tuberculosis examined.—L. i./09, 703.

Opinion is divided as to the presence of the organism in the blood in tuberculosis—work at Brompton did not confirm, *vide*.—L. ii./10, 1747.

The blood of 22 cases of pulmonary tuberculosis examined in all stages and two acid-fast bacilli seen—considered accidental.—B.M.J. ii./00, 1119

**Milk.**—Nearly a quarter of the milk samples from the Metropolitan area were tuberculous.—L. ii./08, 1616; see also p. 341-344. The staining for *B. tuberculosis* is similar to that used for urine. Both the cream and the sediment must be carefully searched on centrifugalising. It is well to soak the slides at the outset after drying and fixing, in ether for a minute or two to remove the fat. Stain by Picric Acid method to exclude butter bacilli. *Negative results in all instances are not necessarily conclusive of absence of infection.* Injection of susceptible animals is then necessary for confirmation.

The Jubilee of Koch's discovery (25 years ago) of the Tubercle Bacillus including note on original method of staining.—B.M.J. i./07, 775.

**Acid Fast Bacteria.** In addition to *B. tuberculosis*, *B. Leprae* (q.v.) and the *Smegma Bacillus* which resists acid by the Ziehl-Neelsen method the following organisms give identically similar reaction.

1. *Timothy Grass Bacillus*. Syn. *Moeller's Grass Bacillus* producing lesions closely resembling tubercles. Another variety of this organism has been found in the dust of hay lofts, and a third variety is known as the 'Mist bacillus' (*Dung bacillus*).

2. The *Petri-Rabinowitch Butter Bacillus* producing lesions closely allied to tuberculosis when injected into the peritoneal cavity of guinea-pigs.

Only in the case of material where outside contamination has been possible do these Bacilli '1' and '2' become an element for consideration—i.e., the customary method of examination is practically of unvarying value.—Muir and Ritchie.

Acid-fast bacilli very common in chronic ear discharges and atrophic rhinitis.—(Wyatt Wingrave, Roy. Soc. Med. Otol. Sec., 1908). They have also occurred in carcinoma of stomach.—Rolleston and Higgs, B.M.J., 1907. Bacilli can be rendered acid-fast by action of fatty acids, e.g., *B. subtilis*, *B. butyricus*, *Clostridia* and *Streptothrices*).

Contrary to public opinion regarding cow's milk as the source of infection, *absence of air and light* from the home and school seems to be the chief etiological factor. Tuberculosis flourishes in not a few countries where feeding with milk from cows or other animals appears unknown.—L. ii./09,284.

The only way for the Local Govt. Board—not local authorities—to effect a complete change in present conditions of supply of milk would be to appoint competent Veterinary Surgeons to examine all dairy farms and to insist that all tuberculous cows be slaughtered, recompensing the farmer—this to come out of National funds, not out of local rates.—Williams, London Pure Milk Association.

The London County Council as far back as 1907 obtained powers to inspect cows in every county to prevent the sending of tuberculous milk to London. The cost has been £4,000 a year. In the first 2½ years 34,000 cows were examined, 534 cases of tubercular disease were discovered and the milk from these animals was kept out of London. Legislation wanted to prohibit the sale of tuberculous milk and to punish offenders.—From the Daily Press, July 12, 1911.

The proportion of tuberculous cows is placed by some authorities at ½ of the entire bovine population.

In all forms of tuberculosis there is bacteriæmia—is the opinion of a worker. The sweeping conclusion that the tubercle bacillus is always present in the blood in tuberculosis cannot be accepted without confirmation.—L. ii./09,1884

Milk and Dairies Bill for Scotland, see P. J. Supp. i./09,391; B.M.J. i./09 1451.

Infection of children with Bovine Tubercle Bacilli. Unsterilised milk in this country is the vehicle by which tubercle bacilli must most frequently be introduced into the bodies of children. Cow's Milk containing bovine tubercle bacilli is the cause of 90% of the cases of tuberculous cervical glands in infants and children residing in Edinburgh and district—in which the research was conducted—and is responsible for by far the larger proportion of tuberculous cervical glands in children during the milk drinking period of life (0 to 5 years). Strong arguments are put forward for protection by legislative measures.—A. Philp Mitchell, B.M.J. i./14,125.

Bread and the spread of tuberculosis. Experiments by mixing tuberculous sputum with the dough. Though the results were negative after baking—in the case of large loaves the temperature in the centre might be insufficient to kill the bacilli.—L. i./13,987.

Prevalence of pulmonary tuberculosis increases considerably in districts exposed to strong Rainbearing Winds, e.g., in those exposed to W., S.W. and N.W. winds. In these districts in England death rate is 1 per 1,000 per annum, and in districts sheltered from these winds the rate is nil. Pr., Jan., '13,300.

Pathogenicity of *B. tuberculosis* stored in normal saline markedly decreased.—L. S. Dudgeon, L. ii./14, 210.

**Opsonins** are non-dialysable proteid substances contained in the serum or plasma of the blood—they are probably formed in the muscle tissue. They possess the power of influencing bacteria in such a way as to render them more easily attacked by phagocytes.

In addition there are said to be bodies variously named agglutinins, precipitins, lysins, and stimulins. To the last named Metchnikoff in particular attributes the power of stimulating the phagocytes to destroy invading organisms. This worker assigns to Opsonins 'a secondary role.



The demonstration of the presence of some such body or bodies by cultivation of (a) Bacterial Emulsion and washed corpuscles compared with (b) Bacterial Emulsion and corpuscles *previously acted upon by Blood Serum* is a comparatively simple and conclusive experiment proving its or their presence.

With regard to the part played by Opsonins in defence some claim that they are allied to the complement of Ehrlich. As now viewed, these bodies do not hold the important place formerly attributed to them by Wright and his school—it is more probable that defensive mechanism against bacteria depends rather upon some unknown enzyme comparable to that elaborated by the organism when any foreign element is introduced into the tissues.

The action of Opsonins is, to a certain extent, independent of quantity, and they are decomposed by heating Serum at 60° C.; on the other hand in the dried condition they will withstand 120° C. Experiments show that there exists a **Preopsonin** which, when necessity arises yields the appropriate Opsonin for a given bacterium.

It is obviously necessary at the outset to determine the nature of the disease to be treated by the examination of the blood or pus.

The **Opsonic Index** for a given organism, *e.g.*, *B. tuberculosis*, is the ratio of the opsonic power of the serum of a patient compared with that of the normal being.

#### **Method of Collecting Blood for Determination of the Opsonic Index.**

Cleanse the index finger or thumb of the hand with a little spirit and water or warm soap and water without using antiseptic. The patient must then swing the arm round from the shoulder a few times so as to concentrate the blood into the hand as much as possible; a bandage or handkerchief is then wound tightly round the second joint of the finger or root of the thumb respectively, and the joint firmly flexed. Should swinging the arm be considered inexpedient, the limb should be held pendant for a few minutes instead. A puncture should then be made near the base of the nail with a lancet, or a flat needle. The finger may then be turned over and the blood allowed to run (the first drops being rejected) into the short end of a **Wright's Tube** or modification of it, which is afterwards sealed at both ends, particular care being taken not to heat the blood. If the finger is not suitable owing to thickened epidermis, puncture the lobe of the ear instead.

Capillary tubes are filled with equal quantities of (i.) **washed blood corpuscles**. For collection of the Blood Cells a suitable pipette is necessary, *e.g.*, made of  $\frac{1}{4}$  inch glass tubing with strong teat attached, and the point drawn out in a fine even capillary tube. A little *Sodium Citrate Solution* 2% to prevent coagulation is first drawn up followed by the blood—the ultimate dilution being about 1 in 6. The corpuscles are then centrifugalised in a centrifuge with hæmatocrite attachment,—(the red corpuscles being heavier are deposited below the white and are rejected), and washed with 0.8% Sodium Chloride once or twice. (ii.) **Suspension of tubercle bacilli**. This in the case of T.B. may be preserved, if killed by heat at 70° C. in a sealed tube, and must be free from clumps, otherwise should be an 18 hours' culture. Ready stained organisms have been suggested for the purpose.—B.M.J. i./07. 866. The strength to be such that 150 to 250 Bacteria appear in the 100 normal cells counted. (iii.) **Serum to be tested**. Equal volumes (Wright) of these are mixed in the capillary pipette and incubated 15 minutes at 37° C. The average number of bacilli ingested per corpuscle is then determined by spreading films by the slide method and staining same with Carbol-Fuchsin, or by Leishman's method for organisms other than tubercle bacilli, the number of bacilli taken up by at least 100 phagocyte cells being counted. *In like manner a determination is made with an equal quantity of a normal serum or of mixed average serum; the ratio is then indicated.* The **Tuberculo-Opsonic Index** in particular has been the subject of considerable investigation. *A lowered index to any organism, whether antecedent or the result of infection, always accompanies the disease in question, and the converse is also true.*

The **Normal Tuberculo-Opsonic Index** has been found to average 0.95. Bulloch found 0.96, Lawson 1.0 and Fleming (*vide infra*) finds normal limits 0.9 to 1.1.

An index below 0.8 or above 1.2 is said to be suggestive of tuberculosis. The index is above 1 in slight early cases, variable in acute cases, below 1 in chronic cases.

Wright explains these by dividing infection into two classes—

(1) *Local*—the opsonic power being permanently low and does not vary.

(2) *Systemic*—great fluctuations and frequently above the normal. On injecting a vaccine there is generally first a diminution in protective substances, *i.e.*, a fall in opsonic power. This is the “negative phase.” Then follows a rise in opsonic power constituting the “positive” phase. By observation it has been proved that an injection should not be given during the negative phase, as that would increase this phase.

The subsequent gradual return to the normal opsonic content may be called the phase of ‘maintained high level.’—Pr. May/o8, 661.

It should be noted that a female infected by any organism shows a marked lowering of the index to that organism at the menstrual period.

The factor in improvement is generally assumed to be a ‘rising’ index.

The duration of the negative phase in phthisis may be a week or more. It seems safest to wait over long rather than inject too soon—the psychological moment has if possible to be found by repeated determination of the ‘index.’ Inject before the fall subsequent to the positive phase which sets in and so make the positive phases accumulate.

*Each phase should be allowed to work out its full advantageous effect generally three weeks or so before the next injection is made.*

Speaking generally, gradually increased dosage is to be employed.

The following is a table of possible results and conclusions to be drawn as to dosage in any case under treatment:—

Index 24 hours after injection.	Index 7 or 10 days later.	Deduction.
Slight fall.	Further fall.	Dose too large, or case unsuitable.
„ rise.	But little altered.	„ too small.
„ fall.	Marked rise.	„ correct.

If there be no alteration at 24 hours or later the dose has been too small. If this be the result a further dose should be given and effect observed.

The fluid portion of pus, and many serous exudations may be almost free from opsonins; in such cases it is necessary to remove fluids lacking in antibacterial power, and to provide lymph rich in such substances. This is done either by opening abscesses, as by tapping an empyema, or by injecting with 0.5% solution of Sodium Citrate with 5.0% of Sodium Chloride to decalcify lymph and induce osmosis.

A fluctuating index after movement, massage, etc., will assist in discriminating tuberculous from non-tuberculous affections.—R. W. Allen.

Fleming points out that the serum of the average ordinary healthy individual to be used as control in Opsonic Index estimations is practically speaking non-variable. Normal serum is therefore a good standard for comparison of infected persons from day to day.

He examined 44 healthy people with 635 estimations: 0.8% being under 0.9, 10.1% between 0.9 and 0.95, 76.7% between 0.95 and 1.05, 10.7% between 1.05 and 1.1, and 1.7% being 1.1. Thus the normal limits are 0.9 to 1.1.

He provides rules for counting the bacteria ingested by the leucocytes, which should be referred to, and summarises his results as follows:—With a diminution of the number of washed corpuscles in the opsonic mixture there is an increase in the amount of phagocytosis. Agglutination of the washed red corpuscles increases the amount of phagocytosis. The tuberculo-opsonic index is the same whether washed corpuscles are used from a healthy or tuberculous individual. If red corpuscles are taken up with serum the amount of phagocytosis is reduced. Serum sealed up in a capsule at room temperature retains its full power, in the case of healthy blood, for at least a week, and, in the case of pathological blood, for a day or two less. Blood capsules left widely open for several hours give very untrustworthy readings. Two practised observers can count the same slides, and obtain results in almost all cases within 10%. Duplicate estimations of the tuberculo-opsonic index of tuberculous patients can be performed, the results differing from each other by less than 20%, except in rare instances (2 in 52).—Pr. May/o8, p 607, 639.

When the body is lowered by disease it still retains a certain amount of reserve resistance, which small doses of devitalised organisms are able to call out. In the preparation of vaccine by devitalising them by heat insufficient to destroy them, objectors have asked how this could be done. Sir A. E. Wright (L. ii./o8, 730) gave an illustration as answer. The body throws into



the blood antibodies or substances which resist anything introduced into it ; e.g., if white of egg be introduced, the blood at once throws off substances to act as antidotes to neutralise it. If the egg-white were heated to a certain temperature it would be devitalised : no chicken could be produced from it, but if introduced into the blood it would still lead to production of antibodies. Estimation of opsonic power forms an incomplete valuation of the protective power but the only possible one to obtain at the present time. Protective power also depends on agglutinating power, phagocytic power of the leucocytes, bactericida and bacteriolytic power of the blood and other factors. Objections has been raised to the opsonic index as being only partial in truth. Sir A. E. Wright says thousands of estimations have shown that there is **a definite correlation between low index and low resistance to disease, as also between high index and curative processes.** It had been said that the index was of no value because patients had died while the index was high—this probably was explained by the fact that the focus of the disease was inaccessible to the blood circulation—“*the protective substances must be brought into effective operation at the site of infection.*”

Emery's Work on Opsonic Index Determination. Leucocytes as the prime factor in immunity (Metchnikoff)—the antibodies and the other substances present in the body fluids play only a secondary role. The Germans, on the other hand, claim that immunity can be explained by the action of Antitoxins and bacteriolysins—though not denying the action of phagocytes. The English School, under Wright, view the phagocyte as the most important agent—but that it only acts, or acts best, in the presence of the special antibody termed ‘Opsonin.’ True Opsonins exist apart from amboceptor—by some thought probably identical.—B.M.J. i./07,496.

Agglutinating, opsonic, bactericidal and bacteriolytic effects can all be obtained independently, i.e., bactericidins, bacteriolysins, agglutinins and opsonins all exist in the blood fluids : of the four, the opsonins are the most important, and they can be accurately measured. Living vaccines are better than killed. In treatment with vaccine the changes which are associated with acquirement of immunity are changes in the blood fluids and not in the white corpuscles. Auto-inoculations, and the comparative methods of treatment by artificially induced auto-inoculations and treatment by inoculation of bacterial vaccines, and the question as to whether these latter may be undertaken in bacterial infections, which are associated with spontaneous auto-inoculations, are discussed, together with a review of results which have been achieved by vaccine therapy. It is doubted whether there is any assured basis for the treatment of bacterial infections by serum therapy.—Sir A. E. Wright, L. ii./07,423,493.

Vaccine therapy applicable not only by means of bacterial vaccines but also by means of judiciously caused auto-inoculations brought about by massage and movements. Satisfactory results not to be obtained by the guidance of clinical symptoms only ; difficulty of estimating approximate initial dose, and deductions to be drawn from clinical symptoms apt to prove fallacious. The greater importance of utilising every other possible means of increasing resisting power of patient and of bringing the immunising forces to the proper point of attack is emphasised—relief of serous effusions, removal of substances such as fibrinous exudate which prevent transudation of lymph laden with protective substances, voiding of abscess cavities, removal of scabs and securing adequate supply of lymph by raising the hydrostatic pressure in the capillaries, and diminishing the viscosity of the blood.—Sir A. E. Wright, Pr. May, 1908.

*The aim being to raise the index, the subsequent doses are given as nearly as possible at the height of the positive phase. In tuberculosis it is not possible to superimpose positive phase on positive phase,—each inoculation is allowed to produce its full effect before reinjecting. In fact the Opsonic Index has been reduced experimentally to 0 in animals by continually re-inoculating during the negative phase. In the case of a healthy person there is no negative phase first but a rise straight away. In diagnosis of tubercle the writer worked out 300 cases with 95% accurate diagnosis.*—P.J. ii./10,76.

Phagocytes considered from the absorption point of view. Quantitative experiments were conducted dealing with the relations subsisting between “Free” and “phagocytosed” bacilli as the concentration of serum or of bacilli altered —L. i./12,228.

### The Opsonic Index as a Diagnostic Method.

A man and a boy were brought into hospital with gangrene of the appendix, it was predicted that the boy would live and the man would die—the prophecy was incorrect. Bacteriological examination showed the serum of the man to give a marked phagocytosis to mixtures of Coli Bacilli, while in the apparently weaker individual phagocytes were almost inert to the same organism—other similar cases showing diagnostic power of the index.—Pr. May, 08,693.

Strictly localised infections, e.g., acne, sycosis, and lupus, may be treated without estimation of the opsonic index. Opsonin and complement probably identical.—B.M.J. ii./08,877.

Estimation of the index in a number of infants under 1 year old (mostly artificially fed) gave the following:—

(a) A low opsonic index is not diagnostic in children under one year old.

(b) In infants a low opsonic index is not inconsistent with health, and the child may be thriving well with a declining index.—Pr. May/08,635.

Extraordinary variations in results of estimation of the index by different workers (all experts with years of practice).—Hort, B.M.J. i./09,400. See also L. i./09,614; B.M.J. i./09,1562.

Opsonic power of serous exudates. Opsonins are not specific bodies.—B.M.J.E. ii./09,16.

Notwithstanding the severe criticisms of the Berlin Pathological Society in 1908, Wright's main conclusions thought to be correct. Many instances are recorded where dose of vaccine was sufficient simultaneously to raise the opsonic index and lower the temperature—recovery following. Detailed directions as to method of estimating the index. For staining the organisms and phagocytes it is thought that the hot solutions of carbol-fuchsin may injure the phagocytes.—L.ii/09,6.

The fall in the tuberculo-opsonic index (the negative phase of greater to lesser degree, according to the dose) produced by a dose of tuberculin occurs either in a healthy or tuberculous individual. In a patient with tubercle constant auto-inoculations are taking place, and each of these is followed by similar fluctuations of the opsonic index. It is clear that in a tuberculous patient observations of the opsonic index to tubercle may show the index to be above or below the normal. Many examinations have to be made before negative diagnosis can be justified.—B.M.J.ii./09,1046.

A positive Index is of undoubted value in diagnosing active pulmonary tuberculosis—a negative index must be taken with reserve. Interpretation of results rests with the clinician.—L. ii./10,1747.

A low Opsonic Index (below 0.8) or a high one (above 1.2) is strongly suggestive of tubercle, but the value of the Index is greatly reduced by the fact that even in tuberculous cases the Index frequently falls within normal limits. Inman has published results showing that this happened in 50% of cases of tuberculosis, therefore even if technique were certain one could only diagnose 50% of cases of tubercle—or less.—Emery, L. i./11,487. See also Serum Diagnosis, Vol. II.

A statistical study of phagocytic distributions as observed by the ordinary opsonic method has shown that no reliance can be placed on single Tuberculo-Opsonic Index determinations which fall within 20% of the mean. Successive determinations essential (though time consuming) but in vaccination such data would be falsified by the rapidly varying antibody content.—B.M.J. ii,10./2035.

Method of estimating strength of a vaccine by a standard bacterial-Emulsion.—J.A. Braxton Hicks, B.M.J. i/12,944.

### Serum Diagnosis of Tuberculosis.—

Application of the Bordet-Gengou Reaction.—Determination of Specific Amboceptor in the patient's serum in treatment with Tuberculins.

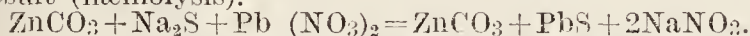
One can, according to Wassermann and Bruck, determine, by means of the complement deviation, the presence of minute quantities of bacterial matter on the one hand and of corresponding antibodies on the other. Tuberculin is mixed with the serum of patients in graduated quantities and a small quantity of fresh normal guinea-pig serum, i.e., complement-containing, is added to each of these mixtures. After an hour at 37° C. a specific hæmolytic serum, previously inactivated by heat is added to each mixture, and then some red blood corpuscles, towards which the serum possesses hæmolytic properties. (The



hæmolytic power of the serum must naturally have been previously determined). If there are any specific amboceptors present in the serum to be examined they will combine on the one hand with the Tuberculin, on the other with complement of the normal guinea-pig serum, hence there will be no hæmolysis as the hæmolysing power of the specific hæmolytic serum necessitates the co-operation of the free complement.

In this way the presence of Antituberculins in the blood of tuberculous patients, at least in such cases as had been treated with specific Tuberculin preparations can be shown and the determination of the amount of antituberculin in the patient's sera gives an index of the degree of immunisation, but the amount of specific immunising bodies will doubtless vary independently in the same way as do the Opsonins. Further, in isolated cases, an observed positive complement fixation has possibly not been caused by the fixation of a specific amboceptor, but through free Tuberculin, as Tuberculin as such, at least in large doses, is in itself complement fixing. Control tests are, therefore, essential.

The reaction amounts to a modified Wasserman Test. Chemists will appreciate the following method of viewing the reaction,—“Let the Bacterium or organism be represented by Zinc Carbonate,—the complement by Sodium Sulphide  $\text{Na}_2\text{S}$ , the immune body by  $\text{H}_2\text{SO}_4$ , Sheep's corpuscles by Lead Nitrate  $\text{Pb}(\text{NO}_3)_2$ . Then  $\text{ZnCO}_3$  and  $\text{H}_2\text{SO}_4$  form a compound which combines with  $\text{Na}_2\text{S}$  forming  $\text{ZnS}$  and  $\text{Na}_2\text{SO}_4$ .  $\text{ZnCO}_3$  cannot combine without intervention of  $\text{H}_2\text{SO}_4$ . Now if to this mixture of bacterium ( $\text{ZnCO}_3$ ), immune body  $\text{H}_2\text{SO}_4$  and complement ( $\text{Na}_2\text{S}$ ) some Lead Nitrate (Sheep's corpuscles) be added no Black Lead Sulphide will be formed (no hæmolysis). But if the immune body be excluded from the mixture a black precipitate will result (hæmolysis).



It will be seen that one molecule of the immune body  $\text{H}_2\text{SO}_4$  absorbs 1 molecule of complement  $\text{Na}_2\text{S}$  in the presence of its specific bacterium ( $\text{ZnCO}_3$ ), and if there is more complement present than immune body some complement (Soluble Sulphide) will remain unabsorbed and will produce blackening with Lead Nitrate, and thus the trace of immune body is likely to be overlooked. In tubercle there are frequently only very small traces of immune body—usually  $\frac{1}{2}$  part of the complement present.—V. B. Nesfield, L. ii./10, 1875. For application to syphilis *v.p.* 322 *et seq.*

The directions in question should be read in conjunction with the criticism of D'Este Emery to the effect that Emulsion of killed Tubercle Bacilli was found better than Tuberculin as Antigen,—the Emulsion to be accurately standardised—*e.g.*, to 4% bacillary substance. The criterion as to the strength of the reaction is the time necessary for the complete absorption of all complement when the Serum and Emulsion are mixed in certain proportions (1 : 4) and incubated—using sensitised human corpuscles. In health the absorption time is 15 to 25 minutes—in 40 tuberculous cases under 2½ minutes. Prognosis is good when the serum contains a large amount of antibody and therefore has a short absorption time. Emery has seen patients improve on a shortening time and *vice versa*,—but this is not invariable. The method has advantage over the eye-destroying counting Opsonic Method.—L. i./11, 56. Further notes by V. B. Nesfield.—L. i./11, 126.

D'Este Emery in reply says practically all persons,—adults especially—have in their blood antibodies to the tubercle bacillus, therefore any diagnostic method must be quantitative, *e.g.*, the estimation of the time in which Complement absorption takes place with an Emulsion of Bacteria of definite strength under standard conditions. All hæmolytic observations on Hecht's method are liable to be vitiated by the fact that the amount of amboceptor is subject to variations as yet unmeasured,—this with the variation in the amount of the complement renders accurate work difficult.—L. i./11, 190.

There are two opposite factors in the process of cure of an infective disease,—on the one hand an increase in the defensive forces tending to cause immunity, and on the other, a specific raising of the sensitiveness of the body to the microbe or its toxin so that it tends to become less immune. The latter process is called ANAPHYLAXIS (opposed to prophylaxis). In the case of tuberculosis the first effect of a tuberculous lesion is to raise the susceptibility of all parts of the body to the tuberculous toxin. This substance,—Tuberculin, is practically without action on a normal person. It is only when he is sensitised by a previous dose or doses that it becomes a real toxin. This

process is in the highest degree disadvantageous to the patient.—the tuberculous fever when not due to secondary infection is apparently an entirely anaphylactic reaction to doses of Tuberculin too small to have any action on a healthy person. It appears however, that this stage is essential to the production of immunity. Both anaphylaxis and immunity are specific—either may serve in diagnosis. The great majority of adults have already acquired some immunity to tuberculosis. Children very commonly have a small tuberculous focus (94% in Vienna amongst the poor become tuberculous before reaching the age of 14) causing no apparent symptoms. Everybody is being constantly vaccinated against the Tubercle Bacillus *via* the alimentary canal and lungs. The traditional peck of dirt must contain innumerable millions of tubercle bacilli. The immunisation or preventive treatment so caused is absent to a great extent in childhood. Adults as a class show sign of having been rendered partially immune to the tubercle bacillus and this renders the diagnosis by the immunity reaction more difficult than in children.—Von Pirquet's test is entirely satisfactory in childhood but of less value in adults—W. D'Este Emery.—L. i./II, p. 485.

THIS ANAPHYLAXIS or INCREASED SUSCEPTIBILITY—the most familiar instance of which is the Serum 'disease' which sometimes occurs after injection of Diphtheria Antitoxin, according to this is an essential feature in bodily response to infection and invasion of the tissue fluids by alien Proteins or Antigens. It forms the basis of the Tuberculin Reaction, since it is only after sensitisation to these substances by previous injection, or by a pre-existent lesion, that the specific reactions occur. Hyper-susceptibility is as much specific as the more obvious or protective immunity. Emery reviewed the various diagnostic methods for tubercle depending on the presence of the various antibodies and pointed out the difficulties with all. A single determination of the Opsonic Index for example is now generally admitted to be only of value if it fall considerably outside the somewhat wide limits allowed (0.8 to 1.2). The Bordet-Gengou Reaction (*q.v.*) is applicable if made quantitative. He modified it by determining the absorption time of complement by Serums in presence of the Antigen which is a standard Bacillary Emulsion, using Blood Corpuscles as indicator—absence of hæmolysis is the index of absorption of complement. In 34 cases of diseases other than tuberculosis and of healthy persons, the average absorption time was 18.1 minutes,—the maximum being 35 and the minimum 2.5. In tuberculosis the average was 7.4 minutes. Absorption times of less than 2.5 minutes were obtained in 25 out of 56 Tuberculous Serums examined. If this time be taken as the criterion the test was therefore obtained in 44.6% of tuberculous and in 8.8% of non-tuberculous—L. i./II, 564, 594.

A. C. Inman on Complement Fixation Test.—L. i./14, 1446.

Precipitation method for estimation of approximate immunity against tuberculosis.—W. H. Fearis, Pr. Apl. 1913, 713.

## **Bacillus Typhosus.—Typhoid Fever.**

Zupink divides bacteria into groups—the organisms of one group will be clumped by the serum from an animal inoculated with any of the same group *e.g.* all acid-resisting bacilli are agglutinated by serum resulting from injecting *B. tuberculosis*. The fact that the agglutinating power of a serum may be exhausted by additions of the bacilli on which it acts proves that the power is in reality due to a definite substance.—Bosanquet.

**Widal's Reaction.**—Collect sample of blood in a small capillary pipette and seal the ends, that nearest the blood being closed first. By pricking the lobe of the ear or the finger the blood will run into the tube by capillarity. The serum is allowed to separate, or the tube is centrifugalised to cause as complete a separation as possible of corpuscles which may mask a reaction. The serum is blown out on to the corner of a slide and a platinum loopful is mixed with 9 loopfuls of normal saline solution, and one loopful of this 1 in 10 dilution is mixed with two loopfuls of typhoid broth, not more than 24 hours old, preferably filtered through ordinary filter paper. This 1 in 30 dilution is now examined as a hanging drop. A control experiment must be conducted in addition.

**Positive Reaction.**—Complete: Clumping of organisms and cessation of movement as a rule in under 30 minutes, or may be instantaneous. Partial reaction. Sluggish movement providing the control is actively motile.



Negative reaction: No alteration in 1 hour. Dilutions 1 in 100 should give same results in 50 minutes; if the time exceeds this the diagnosis is doubtful.

The reaction may also be performed in similar dilutions in sealed capillary pipettes (Wright). This constitutes the macroscopic method of applying Widal's Reaction. For general details see L. ii./03,214.

The urine and other excretions of typhoid patients also possess agglutinative power. It is stated that if the serum be heated to 80° C. for one hour its agglutinative power is lost.

**Notes of Caution in Applying.**—The broth itself or a control with normal serum should first be examined to see that the organisms are freely motile and show no pseudo clumps, as clumps are sometimes present in the broth before the addition of the blood. The serum of persons having previously had typhoid may react even years after. This may cause confusion where a typhoid diagnosis had not been given. Again, if only slightly diluted, e.g., 1 in 10, normal serum frequently 'clumps,' which is not the case on further dilution,—1 in 30 or 50 is safest. Some workers require a result with a 1 in 200 dilution within half an hour to be positive. Too great a dilution may obscure. The blood of *all* cases does not react, case may be too early (generally obtained about end of first week). Cases are recorded where reaction intermits, absent one day, present next, and again recurs, and also a few described where there was no reaction throughout the disease, but these are fortunately very rare.

A special culture should always be at hand—one known to react, as occasionally laboratory cultures do not respond.

A pathogenic organism other than *B. typhi abdominalis* may give the reaction, e.g., according to Durham, *Gartners' bacillus* when mixed with typhoid broth may react. If one drop of blood serum of a patient under infection with this organism (from eating unsound meat) be mixed with 9 of typhoid broth, a positive result may be obtained, but 1 in 100 dilution is negative.—B.M.J. i./98,1797.

Three positive Widal Reports resulted in a diagnosis of typhoid. One proved to be influenza with recovery in three days, the others influenza and lymphadenoma respectively—pointing to the necessity for reviewing other features of the case and the possibility that the patients had been unconsciously subjected to the influence of enteric poison in slight and merely immunising degree.—Douglas Powell L. ii./08,1125.

Blood letting in patients was speedily followed by a rise in the specific agglutinating power of their serum.—B.M.J. i./10,101.

The variability of agglutination of *B. Typhosus* and *M. Melitensis* by normal sera.—L. ii/II,877.

**Typhoid Agglutometer** for early diagnosis of typhoid fever consists of a permanent suspension of dead typhoid bacilli, with apparatus for making a Widal test directly from the blood of the patient without the aid of a microscope. No. 1 is for one test; No. 2 for 15 to 30.—L. i./05,1505.

**Bordet-Gengou Reaction.** This test is claimed to be specific for typhoid. "To conduct the test a susceptible animal is injected with a culture of the typhoid bacillus. This develops amongst other bodies a bacteriolysin *i.e.* the complement, naturally occurring combines with an amboceptor, produced by the liberation from certain cells of the inoculated animal of receptors having 2 affinities, one for the complement and one for the bacilli. The inoculated animal is bled and its serum is obtained after whipping the blood by centrifugalization. The serum is then heated for  $\frac{1}{2}$  hour at 57° C. that is 'inactivated' or deprived of complement. The complement being destroyed, free amboceptors are present in the serum, a measured quantity of which is mixed with some of the original antigen used—*i.e.*, an emulsion of Typhoid bacilli and a measured quantity of the serum of a normal guinea-pig is added. The three constituents are heated about 1 hour at 37° C. By this procedure the amboceptor is enabled to link itself by its cytophile affinity to the bacteria and by its complementophile affinity with the complement contained in such abundance in the serum of a normal guinea-pig. The complement is thus 'anchored' to the amboceptor and is no longer free to combine with any other amboceptor. To this complement another amboceptor is offered, and the inability of the complement to become anchored to another is taken as an indication of the affinity of the first-named amboceptor for *B. typhosus*.

If the inactive serum of a normal animal not immunised against *B. Typhosus* be placed in contact with these bacilli and guinea-pig complement, no au-

choring of the latter body will take place, and it will be free to enter into any other alliance of suitable character available.

If a rabbit be immunised by injecting it, say, with washed red sheep's corpuscles—a hæmolytic serum is produced, *i.e.*, in the rabbit's serum an amboceptor is developed, which by combining with rabbit's complement on the one hand and sheep's corpuscles on the other, produces such an effect that the latter are laked, the hæmoglobin being transfused into the normal saline solution, with which a suspension of the sheep's corpuscles is made. Before exposing the rabbit's serum to the suspension of sheep's corpuscles it is heated to 57° C. In this way the rabbit's complement is destroyed and hæmolytic amboceptors left free, which though capable of combining with sheep's corpuscles, do not in such combination take the latter because no complement is available."—B.M.J. i./09,415. *Vide* also L. i./11,488 and application of the Reaction to Tuberculosis, p. 352.

**Wassermann's Reaction** (*q.v.*) is analogous with this test.

In diagnosis the agglutination reaction has been chiefly used on account of its comparative simplicity, but the fixation or deviation of complement can be and has been used in a great many different diseases to demonstrate the existence of specific anti-substances in the blood and so serve as diagnostic. Thus, *e.g.*, if a small amount of serum (heated to 55° C. to destroy the complement) from a typhoid patient added to a quantity of Emulsion of B. Typhosus the mixture will show the property of absorbing a certain amount of complement, whereas in a control with Normal Serum or with serum from another disease this absorption will not occur.—Prof. Muir, *c.f.*, pp. 326, 327.

Recognition of small quantities of B. Typhosus by complement fixation—in the mixed growth obtained on plates inoculated with an emulsion of fæces.—B.M.J. ii./10,1516.

Diagnosis of enteric fever by the conjunctival instillation reaction.—L. i./12, 313.

**RECOGNITION OF B. TYPHOSUS.**—Gram —. Length 2 to 4  $\mu$ . Long and coccal forms in cultures. Actively motile flagella well seen by dark ground illumination; they may be stained by McCrorie's, Van Ermengem's, or Pitfield's methods, are long and wavy, 12 to 16 in number, though films usually do not show more than 8 to 10, a large number of detached flagella being also visible. No indol production.

The flagella actively motile can be shown by **Pollard's Method** (*vide infra*).

A permanent slight acid production in litmus milk distinguishes from *Gärtner's Bacillus* which produces marked alkalinity in all cultures (milk is not coagulated by either). Neither this, *Gärtner's Bacillus* nor *B. coli*, liquefy gelatin.

Growth on potato translucent (that of *B. coli* and *Gärtner's Bacillus* is brown and moist); in glucose-gelatin no gas formation (differences from *B. coli*, of which many species are known to exist, and *Gärtner's Bacillus*). The Indol test is not always specific with strains of true *B. coli*.

Caffeine enrichment method for separating *B. typhosus* from *B. coli*.—L. ii./05,464; *c.f.*, Bact. Water Examination. *B. typhosus* is said not to grow in a medium containing 0.01% Arsenious Acid, whereas *B. coli* will grow in a medium containing 1.5% of same.

### Flagella Stains.

**MCCRODIE'S STAINS.**—Solution A. Night blue 1 in Alcohol, absolute 20, Alum 1 in water 20, Tannic Acid 1 in water 20. Mix and filter at once. Solution B. Anilin Fuchsin. To 100 Cc. of saturated Anilin Water, add 10 Cc. of absolute alcohol and 1 Gm. of Fuchsin, or Carbol-Fuchsin diluted may be employed.

**VAN ERMENGEM'S STAINS.**—A. 1% Osmic Acid Solution 100, Tannin 18, Water 45. B. Silver Nitrate Solution 0.25 to 0.5%. C. Gallic Acid 1, Tannin 0.6, Potassium Acetate fused 2, Water 70.

**PITFIELD'S METHOD.**—Solution A. Tannin 1, Gm. Water 10 C c. Do not filter. Solution B. Saturated aqueous solution of Alum 10 Cc., saturated Alcoholic Gentian Violet Solution 1 Cc. Filter and keep in a stoppered bottle. Fuchsin will answer the same purpose as Gentian Violet. Equal parts of A and B mixed, heated to nearly boiling and employed to stain 1 to 3 minutes, wash in water, dry and mount.

**POLLARD'S METHOD.**—Young agar cultures not more than 24 hours old of a motile micro-organism are employed. An emulsion is made in about 8 Cc



of tap (not distilled) water. Six drops of fresh 5% Tannin Solution are added. After  $\frac{1}{2}$  hour a turbidity will be noticed. Shake gently and examine 'hanging-drop' with  $\frac{1}{2}$  inch objective, this shows the organism with flagella attached, especially round the edge of the drop. Numerous active detached flagella are also visible.

These preparations may be dried and stained by (i.) Simple stain, e.g., Carbol fuchsin or methylene blue; (ii.) Ziehl Neelsen's method. Good results can be obtained with cultures even a year old, in the latter case, however, the organisms are generally non-motile.

*Differentiation of B. Typhosus from B. Coli and other similar organisms:—*

Gärtner's *Bacillus* thought to be a modification of *B. coli*, and the above differences not always constant, and even the agglutination test between *B. typhi abdominalis* and *B. coli* not always reliable. Stab and stroke cultures on agar containing 0.3% glucose, stained with neutral red, distinguish *B. coli*, discharging it probably because it is a strong reducing agent, producing a saffron tint with fluorescence in 12 to 24 hours, but *B. typhi abdominalis* is without action on the red tint.—L. i./oi,613; P.J. i./oi,391.

*B. coli communis* is a normal and advantageous inhabitant of the intestine, but may become responsible for an attack of inflammation of the bowel or epidemics of food poisoning.—P.J. ii./o3,740.

"**Krystall Violet**" and neutral red, advocated for distinguishing colonies of *B. coli* (coloured red) from those of *B. typhi abdominalis* (also *B. enteritidis* Gaertner and others), coloured blue to purple. Medium contains Sodium taurocholate to inhibit growth of nearly all but intestinal bacteria. Lactose is another essential component of the medium, as *B. coli* and congeners decompose it with gas formation.—B.M.J. i./o2,1473.

Conradi evolved a method of early diagnosis of typhoid fever. Researches demonstrated necessity of keeping the blood in a fluid condition, so as to avoid the disinfectant action of those substances which become active on coagulation. Bile is employed for this purpose; in addition, the medium contains 10% peptone and 10% glycerin. The blood from lobe of the ear is drawn into a pipette containing a little bile and mixed with two or three Cc. of the Peptone-glycerin-bile medium in the proportion: blood 1, medium 3. Incubate at 37° C. for 10 to 16 hours and make cultures on agar plates according to the **Drigalski-Conradi formula**, q.v. p. 253. Diagnosis can be effected by this method in 26 to 32 hours, and it is applicable as soon as the patient exhibits a febrile temperature.—B.M.J. i./o6,339.

Brilliant Green has been found of service in the elimination of *B. Coli* from cultures which have to be searched for *B. Typhosus*.—P.J. i./14,592.

With regard to persistence of this and other organisms in London water see p. 260.

Persistence of typhoid bacilli in the kidney after apparent recovery from typhoid—and the Widal reaction also given.—B.M.J. ii./o7,75.

The bacillus could be recovered from bottles intentionally infected with it, in course of an investigation on best mode of disinfecting water for military use, even after washing out 12 times with sterile water.—B.M.J. ii./o7,518.

Sunlight (in India) reduced 240,000 typhoid organisms in  $\frac{1}{2}$  hour to 1,000, in 1 hour to 5, and in 2 hours to nil.—L.i./o9,742.

**VITALITY OF B. TYPHOSUS.**—There is considerable difference between the vitality of the organism when grown on artificial culture media and the capacity of the same bacillus for survival under natural conditions. The culture bacilli possess much greater vitality than organisms obtained directly from excreta.—B.M.J. ii./o9,482.

**MAY GRUNWALD'S SOLUTION** is a Methylene Blue—Eosin Mixture similar to Jenner's Stain for typhoid diagnosis.—B.M.J. ii./o6,1848; B.M.J.E. ii./o6,77.

**B. paratyphosus** (*Brian and Kayser*), *Paratyphoid* in the tropics (Ceylon). The disease is indistinguishable from typhoid, though generally running a milder course. Intestinal ulcers are identical with those of typhoid. Cases of mixed infection are not rare.—L. i./o7,284, 1293, 1571.

Distribution of certain bacilli of the food-poisoning group (*B. Suipestifer* and *B. Paratyphoid* ('B.)) more limited in England than abroad.—B.M.J. ii./10,1503.

Variation among bacteria. The author describes a bacillus which was isolated from a former typhoid carrier, and which formed acid but no gas in glucose media, and which fermented lactose at 22° C. but not at 37° C. In not developing gas in glucose media, but forming some Mannite it resembles

certain Colon Bacilli of the "anærogenes" class which form connecting sinks between *B. Coli* and *B. Typhosus* group of micro-organisms.—B.M.J. ii./10,1909.

Paratyphoid and Meat Poisoning.—F. A. Bainbridge, Lecture I, L. i/12,705; Lecture II, L. i/12,771; Lecture III, L. i/12,849.

**Fermentation Reactions of *B. Typhosus*.** Investigations gave the following conclusions:—

(1) The fermentation reactions of *B. Typhosus* are identical up to the 4th day. (2) *B. Typhosus* ferments glucose, mannitol, galactose, and sorbitol with the formation of acid within 24 hours. Dulcitol\* and arabinose are fermented more slowly, acid being produced usually during the second or third week. Lactose, saccharose, dextrin, inulin, amygdalin, salicin, raffinose, erythritol and adonitol are not fermented. Gas is never produced by *B. typhosus*. Litmus milk is turned faintly acid generally within 24 hours, and remains thus permanently. (3). The time taken to ferment dulcitol or arabinose varies widely even in the same culture tested repeatedly, and also amongst daughter colonies from a single-plated culture. (4). The time taken by a given strain of *B. typhosus* to ferment dulcitol or arabinose is very markedly quickened for that strain by a sojourn in media containing dulcitol or arabinose respectively. (5). Within certain limits the increase in (dulcitol) fermenting powers varies with the length of sojourn in dulcitol-containing medium. (6). The increased activity as regards fermentation of dulcitol persists through several generations of agar cultures, but eventually tends to die out. It also persists on stored agar cultures for over a month if this culture be sub-cultivated and tested. (7). No other modifications either as regards agglutination, fermentation reactions or cultural characteristics are seen in the agar cultures after passage through dulcitol (or arabinose) containing media other than the increased activity towards the corresponding "sugar." The cultures after passage through dulcitol become "dulcitol active," and after passage through arabinose "arabinose active." The "dulcitol active" cultures do not show any increased activity towards Arabinose, nor do the "Arabinose active" cultures show any increased activity towards dulcitol. (8). Mere passage through peptone water or through other sugars, *e.g.*, mannitol, lactose, or saccharose—does not increase the fermentative activity towards dulcitol or arabinose. (9). It was not found possible to make *B. typhosus* ferment lactose or saccharose. (10). By means of passage through appropriate sugars it was found possible to develop two modifications of an anærogenic coliform organism each active towards a new sugar not easily affected by the original strain. (11). The fermentation activity of *B. typhosus*, while one of remarkable constancy in quality, can be increased in quantity and suggests that certain work of classification amongst colon organisms requires reconsideration.—Bradley, P.R.S.M., Dec. 1910.

W. J. Penfold dealing with fermentation of Lactose Peptone Water and of Dulcite Water by *B. Typhosus*, states it does not ferment Arabinose. Fermentation of Glycerin and papillæ formation on Isodulcite.—B.M.J. ii./10,1672.

TYPHOID CARRIERS cannot be said to be cured until daily examinations of the fæces demonstrate absence of the bacilli for a period extending at least from April to November.—L. ii./08,1589. For a number of other references see Edn. XIV., p. 816, also Na. Dec. 1 10,45.

Typhoid germs 38 years in the body.—M.P.C. ii./11,584.

Enteric fever carriers,—on a basis of three persons liable to excrete Typhoid Bacilli per 1000 of population London alone would contain more than 14,000 carriers. The total number of known enteric fever cases in London in 1908 was only 1,357. Carriers however numerous have not prevented the conspicuous decline which has taken place in the prevalence of enteric during the last half century—hence the danger of the average carrier would appear negligible,—measures at present employed in the prevention of the disease seem adequate to cope with the 'carrier' also.—L. ii./10,1631.

\*Dulcitol is synonymous with Dulcite and Melampyrite  $C_6H_8(OH)_6$ , a sugar from *Melampyrum nemorosum* and other *M.* and *Euonymus* species. It occurs in white crystals soluble in water, slightly in alcohol.



Bacteriology of human bile with especial reference to the typhoid carrier problem. Of 100 Cases 23 were sterile, in 51—or a half—*B. Coli* was isolated in pure culture. *B. Coli* is more frequently found when death is due to intra-abdominal disease than when it is due to affection of other parts. It was, for example, isolated in every case except one, in which death was attributed to appendicitis or peritonitis, but was not once found when it was due to cardiac disease. In only four cases were bacilli of the typhoid-paratyphoid group isolated. There are at large individuals never supposed to have had typhoid fever who are in reality chronic typhoid carriers.—Q. Jl. Med. Jan. 1911.

**Flies as Typhoid Carriers.** Investigations show that if injected into the flies' intestines they can be recovered as long as six days afterwards. The bacilli were found in the flies' faeces during the space of two days. Similar results with Gaertner's *B.* but the bacilli were not recovered from the faeces.—B.M.J. ii./10,1271.

Flies in relation to typhoid fever, dysentery, etc. Prof. C. J. Martin concludes:—The facts brought forward in the statistical paper do not necessitate recourse to the hypothesis that carriage by flies dominates the situation. The fly hypothesis is the only one offering a satisfactory interpretation of the extraordinary dependence of the epidemic upon the accumulated effect of temperature. It offers further a ready explanation of the spread of infection to neighbouring children who have no direct personal contact with the patient. Peculiarities of the relation in times between fly prevalence and the epidemic in different localities are not inconsistent with the view that fly carriage is essential to epidemicity. No other interpretation so far forthcoming is nearly so satisfactory.—B.M.J. i./13,1; L. i./13,1.

Cattle and horses as typhoid carriers may explain the erratic behaviour of this disease.—L. ii./12,1543.

**B. Enteritidis Sporogenes** (*Gaertner*).—An anaerobic organism staining by Gram's method, spores only on blood serum (?), which it liquefies. Note on, found in the dejecta of the sufferers in the epidemic of diarrhoea at Bartholomew's Hospital in 1895. Detection of in water supplies.—P.J. i. c2,25.

Said to be the cause of infantile diarrhoea. Growth in milk produces characteristic separation of stringy curd and excessive whey. Extremely pathogenic to guinea-pigs from which pure cultures obtainable from the oedema fluid by growing on blood serum under anaerobic condition, *c.f.* Water Examination, p. 259.

A Gram — variety the cause of outbreak of meat poisoning at Limerick which produced 9 deaths. The outbreak indicates danger of private slaughter-houses and lack of supervision; secondly, the necessity of thorough boiling of economically 'left-over' pieces of meat, especially beef, if they have to be 'used up.'—B.M.J. i./09,1171.

## **Typhus Fever.**

Animal inoculations (monkeys) succeeded for the first time—previously the disease was regarded as special to man. The transmission was effected by 1 Cc. of the blood from a typhus case injected into a young chimpanzee—typical attack after 24 days. The virus in the blood of this animal was found to be increased in virulence. Injected into a macaque the disease developed in 13 days—blood from this injected into others reduced incubation period further. Other types of *macacus*, also dog and white rat were proved immune. The serum of a macaque convalescent was found to be toxic. Human body lice fed on typhus-monkeys infected other monkeys.—C. Nicolle—Annals de l'Inst. Pasteur, *per* L. ii./10,182.

Ætiology of—a résumé of knowledge to date.—L. ii./11,172. The fever can be excited in apes by injection of the blood of a patient suffering from "tabardillo," which is typhus as it occurs endemically in Mexico, and the virus uncultivable and invisible, even with dark ground illumination, did not pass through a Chamberland or Berkefeld filter. One attack of fever produced by inoculation protects against a second infection. Nothing has been grown from the blood on media. Lice—*pediculi vestimentorum*, are thought to possibly carry the infection. See also B.M.J. i./13,64.

Collected studies on typhus fever. Etiology of Tabardillo (the typhus fever of Mexico) discussed.—Review, L. i./13,1172.

### **Bacillus Vaginæ, Döderlein's.—**

An aerobic organism, Gram —, often feebly +, constantly found in the normal vaginal secretion in adults. Facultative anaerobe, non-motile, non-pathogenic.—Gould.

In a series of examinations of the vaginal secretion in infants this organism was absent. In more than half the cases (ranging from 30 minutes old to 13 days) the fluid was sterile. The reaction of the secretion is (normally) acid in the majority of cases,—not due to action of micro-organisms. Amongst the organisms found were a yellow *Staphylococcus liquefying* gelatin and white *Staphylococci* not liquefying.—P.R.S.M. Obst. Sect. Nov. 10, 26.

*B. Vaginæ* is the only definite micro-organism of the vagina. It plays the important role of preventing the development of other micro-organisms, especially those of a pathogenic kind by the production of Lactic Acid.—B.M.J. ii./10,1222.

**Yellow Fever.**—If the blood of a yellow fever patient be filtered through a finely pored Pasteur-Chamberland porcelain filter the filtrate on injection will still transmit the disease showing the existing of micro-organisms which cannot be seen by the ordinary microscope.—Hewlett, P.J. i./13,250. The germ of the fever is generally believed to be a protozoon, ultra-microscopic.—L. ii./10,1527. Infection of the disease is probably carried by *Stegomyia fasciata*. *Filaria Bancrofti* has been regarded as the specific germ—it has its permanent host in the mosquito, undergoing sexual reproduction in the human blood—the exact reverse of what takes place in malaria—in which man is the permanent host, the germs of yellow fever must, therefore, be searched for in the mosquito. A bacillus designated the *Bacillus icteroides*, has been found in the disease, but this is not the important feature.

The infected insect lives a long time, and it can transfer the fever as long as it lives—59 days has been recorded. It hibernates in the United States; but, if the infected adult insects hibernate, either a very large proportion of them die or else the infecting parasite must generally die in the mosquito—the first seems probable.

The cycle of the yellow fever parasite in the mosquito before it is communicable to man is about 14 days. C.f. also B.M.J. i./05,552.

Proof of endemic origin of yellow fever in West Africa. It is claimed that the final proof that remittent and bilious remittent fevers are in many instances the mild forms of yellow fever will be given when by the destruction of *Stegomyia* these fevers will disappear in great part with yellow fever.—Sir Robert W. Boyce.—B.M.J. ii./10,1771.

History of Yellow fever,—it is endemic amongst natives of the coast towns. Rational precautions of segregation and *Stegomyia* destruction necessary to prevent great set backs to commercial progress in West Africa. Evidence is overwhelming in favour of the disease being endemic on the West Coast of Africa, and of its having been repeatedly mistaken for other diseases (often called “bilious remittent fever”) or entirely overlooked, and of its being kept up in a mild form by the natives and infected by *Stegomyia*.—B.M.J. i./11, 491,249,301.

### **YELLOW FEVER ON WEST COAST OF AFRICA, DISCUSSION ON.**

If not a natural immunity, many natives have at least an acquired one,—probably through mild and frequent attacks sustained in childhood. The endemicity considered by many as an established fact. Cases are described of “whites” usually having some slight “disorder” on their first visit to places endemic to yellow fever, many factors point to this “disorder” being a mild form of yellow fever, which would account for the immunity enjoyed afterwards by these people.—B.M.J. ii./11,1263; L. ii./11,459. Etiology of, L. i./12,183.

Yellow fever in Yucatan (Mexico). The natives are assumed to be immune from childhood. Relationship of *paraplasma flavigenum* to the disease.—L. ii./12,1812,1830.

A recent *résumé* of researches on, *vide* L. i./14,1408,



**Whooping Cough.**—Bordet's *Bacillus*.—A cocco-bacillus, non-motile, Gram-negative, staining feebly, regarded as causative of whooping cough, has been isolated. Cultures of the organism were found to be specifically agglutinated by the serum of children suffering from. Agglutinating reacting of the serum is not strong.—B.M.J. ii./09, 323, 1062 (complete paper); L. ii./09, 471. See also Vol. I. p. 933 and Therapeutic Index.

**Gram's method of differentiating Organisms in Film Preparations:**—

1. Anilin-Gentian-Violet 3—5 mins. 2. Without washing, Gram's solution  $\frac{1}{2}$  to 1 min. 3. Pour off Gram's solution, wash in water, rinse with alcohol, three times, each of 10 seconds duration. Counterstain with neutral red 0.5% or weak Carbol-Fuchsin  $\frac{1}{2}$  minute. 4. Wash in water. Dry.

Gram's Iodine solution has the formula:—Iodine, 1 Gm.; Potassium Iodide, 2 Gm.; Water, 300 Cc.

**NOTE.**—Anilin-Gentian-Violet is prepared by adding 1 part of a concentrated alcoholic solution of the dye to 9 parts of a filtered saturated solution of anilin oil in water (solubility about 1 in 30). P.G.V. directs 7 Cc. of the Saturated Alcoholic Solution of Gentian Violet with a further 10 Cc. of Absolute Alcohol to be added to 100 Cc. of filtered Anilin-Water. This may overcome 'muddiness.'

**Gram-Eosin Method for Sections.**—1. Place a little alcohol on section  $\frac{1}{2}$  min. 2. Cover with filtered Anilin-Gentian-Violet 10 mins. 3. Gram's solution, 3 mins. 4. Decolourise in Alcohol. Wash in water. 5. Stain with Eosin 1—2 mins. Wash in water. 6. Dehydrate with Alcohol. 7. Clear with Xylol, mount in Xylol Balsam.

**Eosin-Gram-Weigert-method.**—Eosin (5% aqueous) 5 to 10 mins. Wash in water. Anilin-Gentian-Violet 10 minutes without washing. Gram's iodine solution, 3 minutes. Wash in water. Blot, dehydrate, and differentiate in anilin oil until pink colour returns. Clarify in Xylol and mount in Xylol Balsam. This method is preferable to the Gram-Eosin method, as anilin oil is more gentle in decolorising action than the alcohol used in the latter.

A simple stain for sections is:—

**Carbol Thionin Blue.**—Thionin Blue, 0.65 Gm.; Absolute Alcohol, 3.5 Cc.; Phenol Solution, 5% 39 Cc.

**Carbolic Methyl Violet.** *Syn.* Carbol Gentian Violet.

This is better than Anilin Gentian Violet especially in hot climates. The Methyl Violet Stain is:—Melted Carbolic Acid 12.5 Cc., Absolute Alcohol 25 Cc., Methyl Violet 6 B. 1 Gm. Dissolve, keep in a warm place 24 hours and filter. Fix the smear with Alcohol. Place 3 or 4 drops of Distilled Water on the smear and one drop of the stain. Then Gram's Solution in the usual manner. Counterstain with Safranin or weak Fuchsin.—B.M.J.E. i./13, 96.

Anilin dyes exhibiting the most powerful lethal action on a typically Gram + staining micro-organism (*Staphylococcus*) are those which can be used with the greatest success by the method. Substances having special affinity for the dyes in question are assumed to be present in Gram + staining organisms and as Iodine plays a special role in the Gram reaction, special examinations with *lipoid* substances gave interesting data. (1) Treatment of *B. Coli* with Lecithin Emulsion may make it Gram + staining. Boiling *Staphylococci* with Ether renders them almost entirely non-Gram staining.—Jl. Path. & Bact.—July, 1911, p. 146.

We found that non-Gram staining organisms were decolorised in periods varying from 2 to 5 minutes, using strong Methylated Spirit, and that Gram staining organisms were not decolorised even after one hour's washing. If weaker spirit, e.g., 60%, is used, organisms that were not decolorised in an hour with strong spirit may be almost decolorised in ten minutes, therefore the strongest Spirit is absolutely necessary. The Iodine treatment should be for at least 5 minutes, in fact it cannot be overdone in a film preparation. We should recommend 10 minutes washing with the Spirit.

List of some pathogenic and common non-pathogenic organisms stained and not stained by Gram's method:—

A. STAINED (' + ').	B. NOT STAINED (i - ).
Staphylococcus, all varieties.	Bacillus mallei.
Streptococcus pyogenes.	,, typhi abdominalis.
Micrococcus tetragenus.	,, coli communis.
Fraenkel's pneumococcus.	,, coli dysenteriae.
Bacillus Acne.	,, enteritidis (Gärtner).
,, anthracis.	,, pestis.
,, botulinus (Acne).	,, pyocyaneus.
,, diphtheriae.	,, influenzae.
,, enteritidis (Klein).	,, Friedländer's Pneumo.
,, Oppler-Boas.	,, Malignant oedema.
,, pseudo-diphtheriae.	,, Symptomatic anthrax
,, xerosis.	(Charbon).
,, tuberculosis.	,, prodigiosus.
,, Smegmæ (? -).	,, proteus vulgaris.
,, lepræ.	,, fluorescens liq. and non-liq.
,, subtilis.	,, Smegmæ.
,, Welchii.	,, soft sore.
,, tetani.	Diplococcus intracellularis meningi-
Aspergillus.	tidis.
Sarcinæ, all varieties.	Diplococcus Catarrhalis.
Yeasts (Blastomycetes).	Gonococcus.
Ringworm Fungi.	Spirillum cholerae Asiatic.
Streptothrix of Actinomycosis.	,, Metchuikovi.
,, of Madura disease.	,, Finkler and Prior.
	Spirochetes of Syphilis, Relapsing
	Fever, Vincent's Angina, and
	other parasitic protozoa.

**Nitrobacterin.**—Nitrifying bacteria on the nodules of leguminous plants (peas, beans, clover, &c.) are cultivated under this name for enriching soil. The sequence of crops is turnips, barley, clover, wheat. Practice has been ahead of science. Some other valuable and concise information as to the bacteriology of fermentation, caseination, &c.—B.M.J. ii./07, 1764.

**Semen Test.**—The presence of spermatozoa may be detected by evaporating a drop of the liquid from the moistened stains, fixing it by a flame and staining with eosin and methyl green. At the base of the head of the spermatozoon is a hemispherical portion which stains green, while the anterior part and tail stain red. Some prefer the use of methyl green alone. Ehrlich's Hæmatoxylin (stain 5 minutes) wash in distilled water, then in tap water until blue, and counterstain with Eosin solution (2 or 3 minutes), also gives good results.

**Semen Stains** may be identified by boiling (fabrics) 2 minutes in a watery solution containing Tannin  $\frac{1}{2}\%$  and Sulphuric Acid 1 per 1,000, then wash with strong Ammonia Solution 1 in 400 for 2 minutes, immerse 5 minutes in a solution of potassium bichromate 1 in 10,000 with 1 in 1,000 Sulphuric Acid, transfer for 2 minutes to 2% Potassium Cyanide Solution; finally rapidly wash in distilled water. Scrape and tease up on a slide, dry, fix, and stain.—B.M.J. ii./06, 1261, 1843.

**Semen Stained by Eosin.**—Cut a portion of the cloth  $1 \times 1\frac{1}{4}$  inch, soak in Müller's Fluid 24 hours preferably at  $37^{\circ}$  C. in incubator (e.g., in covered watch glass). Wash in several changes of water to remove dirt and also fixing fluid. Place the cloth, one end held in forceps, for a moment on blotting paper to remove excess of moisture, then lay flat on centre of micro slide. Pass edge of scalpel or of another slide with a fair amount of pressure from the end of the cloth fixed by the forceps, to the other. Repeat on the other surface, turning the cloth over on the same portion of the slide. The end of the cloth is then placed, with the forceps between finger and thumb, the rest being pleated up by the same means and tucked in so that firm pressure of the tips of forefinger and thumb causes a drop of liquid to fall which add also to the slide. Dry in incubator, and stain three minutes with 1% Eosin solution.—B.M.J. ii./08, 501.



**Picric Acid Test for.**—Mix the suspected semen, whether liquid or dry, with a little water, add a drop of Glycero-Solution of Picric Acid containing a little alcohol—if human semen, yellow needle crystals, visible under the microscope.—M. 1906.

### Preparation of Sections before Staining.

**Rapid Paraffin method** for small pieces of tissue. Fix in Alcohol two hours, Acetone 1 hour, Anilin Oil  $\frac{1}{2}$  hour, Xylol  $\frac{1}{2}$  hour in the Incubator at  $37^{\circ}$  C.—then in Paraffin at  $\frac{1}{2}$  hour  $70^{\circ}$  C.

**Slow Paraffin method.**—Fix in Alcohol (not Formalin) 2 days, then place in Xylol 3 to 5 days.

N.B.—Tissues fixed in Formalin or Müller's Fluid must be thoroughly soaked or the sections will not adhere to slides. Use fresh (unused) Paraffin for embedding. To fix frozen sections to slide damp off excess of water with filter paper, flood three times with Alcohol, then once with 0.5% Celloidin in Acetone. Then stain.—Wyatt Wingrave.

**Rapid Gum-freezing.**—Place tissue into boiling Müller's Fluid or Formol-Müller, or plain water. Boil 3 minutes, wash in water; freeze in Gum with Ethyl Chloride or by Carbon Dioxide.

**Müller's Fluid.**—Potassium Bichromate  $2\frac{1}{2}$ , Sodium Sulphate 1, Water 100. Is used in histology for hardening tissues.

**Formol-Müller Fluid.**—Müller's Fluid 100, Formalin 5.

**Erlitzki's Fluid.**—Potassium Bichromate 5, Copper Sulphate 1, Distilled Water 100,—used in the same way as Müller's Fluid. Microscopical examination of the eye, Method and formulæ.—Oph. 1911, 781, 842.

**Transparent method** for bony specimens.

Dehydrate in successive baths of Alcohol and Acetone, Anilin Oil, Xylol, and Liquid Paraffin.

**Formalin Preservative Solution.**—Formalin (40%) 78, Potassium Acetate 3, Potassium Nitrate 1, Glycerin 40, Water 140.

This has the advantage of retaining the colour of pathological specimens.

Method of cutting frozen sections of fresh tissues for immediate microscopic diagnosis during operations. Lockwood & Shaw.—B.M.J. i./07, 127.

**Frost's Solution** for preserving anatomical specimens. Sodium Fluoride 80, Chloral Hydrate 80, Potassium Acetate 160, Cane Sugar 3,500, Saturated Thymol Water 8,000. The specimens retain life-like appearance L. i./12, 579.

**Farrant's mounting medium.**—Gum Acacia, best small, 32 ozs., wash well with 6 ozs. of water in two or three lots and dissolve in 40 ozs. of boiling water with constant stirring. Strain through muslin and add Arsenious Acid 1 drachm in Glycerin 40 ozs., heat gently to clarify.

**Apathy's Gum Syrup. For ringing Slides**—Picked Gum Arabic, Cane Sugar (ordinary, not candied), Distilled water, of each 50 Gm. Solve in water, and add 0.05 Gm. Thymol. Render alkaline with a little Sodium Carbonate. This sets in about 15 to 30 minutes in a warm room. The use of this with other precautions, helps in preventing slides from fading.—L. i./11, 877.

### CULTURE-MEDIA FOR BACTERIOLOGICAL INVESTIGATION.

**Nutrient Broth.**—Boil 'Lemco' 5 Gm., Peptone 10 Gm., Sodium Chloride 5 Gm., Water 1,000 Cc. Make faintly alkaline with dilute Sodium Carbonate solution, using litmus as indicator, and filter through grey paper. The broth thus prepared may be run into specially cleaned test-tubes, about 5 Cc. into each. These are now plugged and sterilised at  $100^{\circ}$  C. for a quarter of an hour on three successive days, or the broth may be converted into other nutrient media.

The following is sometimes used:—Beef (or horse, &c., flesh) 450 Gm. freed from fat and minced, is extracted for twenty-four hours with cold water 1,000 Cc. The albumin is coagulated by heat and strained off. The re-

sulting extract is boiled ten minutes with Sodium Chloride 5 Gm., and Peptone (in powder) 10 Gm., with occasional shaking. Finish as above after rendering alkaline.

**Standardisation.**—The broth and the gelatin and agar media made from it are acid to phenolphthalein, but are frequently neutral or even alkaline to litmus—this latter not being sensitive to many of the weak organic acids present in the meat extract. The medium is, therefore, standardised with  $\frac{N}{10}$  soda in the presence of phenolphthalein. The reaction of a medium is usually expressed by the number of Cc. of normal alkali required to be added to 1 litre of medium to render it exactly neutral to phenolphthalein *e.g.*, ' + 10 ' indicates that 10 Cc. of N soda have to be added to neutralise it. *This reaction has been found best for general bacterial growth, and is the standard employed.* The rule for standardising, therefore, is to subtract 10 from the number of Cc. of normal soda that must be added per litre; for example, if 10 Cc. of a medium require 1·2 Cc. of  $\frac{N}{10}$  soda, then 1,000 Cc. = 12 Cc.  $\frac{N}{10}$  soda. The medium is now neutral to phenolphthalein, but distinctly alkaline to litmus. Then subtracting 10 Cc. from 12 we have 2 Cc. of  $\frac{N}{10}$  soda to be added to 1 litre of medium.

**Glucose Broth** consists of Nutrient Broth with the addition of 1 or 2% of pure anhydrous glucose added after final filtration, but prior to sterilisation.

**Glycerin Broth.**—Nutrient Broth containing 5 to 8% of Glycerin.

**Litmus Broth** consists of the addition of a sufficient quantity of Litmus solution to neutral broth to render it distinctly blue in colour.

**Nutrient Gelatin.**—Broth 1,000 Cc., gelatin 125 Gm. Melt in steamer, and clarify by adding the white of one egg, to which a little water may have been added, render faintly alkaline, place in steamer to make quite hot, and filter in the same, leaving the portion containing the coagulated albumin, which will have subsided, carefully until the last. Run the medium into tubes, about 5 or 8 Cc. into each according as to whether 'slopes' or 'stab' preparations are required. Sterilise on three successive days.

**Glucose Gelatin** consists of nutrient gelatin to which 1 or 2% glucose has been added after filtration. For the cultivation of anaerobic organisms and to observe gas formation. Must not be sterilised in the autoclave.

**Nutrient Agar.**—For this medium the following gives satisfactory results:—Nutrient broth 1,000 Cc., powdered agar-agar 20 Gm. (passed through a drug-mill and made as fine as possible); melt in the steamer, or better in an autoclave, allow to cool slightly, or, if time is an object, cool by shaking under a stream of cold water from the tap; add white of two eggs, *make just alkaline*, boil in the steamer or autoclave twenty minutes, and then transfer to a tall beaker; allow to get quite cold, remove the solid mass from the beaker, and cut off the bottom of the block of jelly containing the coagulated albumin and sediment. The remainder is again thoroughly melted in the autoclave or steamer, and will then filter well (in the steamer). It may be poured into tubes, and sterilised in the autoclave for a quarter of an hour under a pressure of at least two atmospheres—or, in the steamer on three successive days. Instead of cutting off the sediment on setting, it may be kept out by straining the hot liquid through butter-cloth previous to filtration.

N.B.—The white of egg should be added when the medium has almost set—*i.e.*, as cool as possible—as the albumen coagulates at 65° C. and it acts purely mechanically by carrying down with it the particles of suspended matter.

**Neutral Red Egg Medium** (Fleming's) for cultivation of Staphylococci from the urine. Differs only from Dorset's in that it contains 0·005% Neutral Red as an indicator.

**Dorset's Egg Medium.**—The contents of 4 fresh eggs are well beaten and 25 Cc. of water added, the mixture strained through muslin to remove air bubbles, then tubed (or plated) and heated 4 hours at 70° C. It may be further sterilised by heating in the autoclave for 5—10 minutes at 105° C. The addition of sufficient basic Fuchsin to colour the medium slightly pink enables early growths to be more easily seen.—M. & R., 6th Edn., p. 45.

H. Warren Crowe's procedure for the preparation of Neutral Red Egg Medium is as follows:—He places the requisite amount of Neutral Red (25 Cc



of 0.01% aqueous solution of Neutral Red for each egg) in a flask plugged with wool, and autoclaves it together with two rubber corks, one with two wires or glass rods long enough to reach within one inch of the bottom of the flask, the other carries two tubes, a short one reaching two or three inches from the cork on the inside and fitted with a hooded pipette on the outside, and one reaching to the bottom of the flask, the outer portion being bent to form a recurved angle and plugged with wool. He then soaks the eggs in spirit, flames them and cracks them at each end with long sterile sinus forceps, breaking the yolk by pushing them in and opening them inside the egg. When all the eggs are in, the rubber cork with the rods is placed in position and the contents of the flask emulsified by shaking (the rods serve this purpose). The flask is then inverted, suspended and allowed to stand until the whole of the particles of egg-shell, *etc.*, have settled below the level of the shorter tube. The medium is then ready to run into tubes or plates, which are finished by heating to 90° C. for half an hour.—P.R.S.M., Path. Sect.—Vol. VI., p. 117; L. i./13,1377. See also *Rheumatism, Vaccine Therapy, Vol. I.*

**Musgrave's Medium.**—Beef Extract 0.5, Sodium Chloride 0.5, Agar 20, Tap Water to 1,000. Alkalinity minus 1 gives a growth of fairly constant characters. Employed in growing coli-form bacilli from patient's bowel in making autogenous vaccine (for treating goitres).—L. i./13,1371.

**Blood Agar** is prepared by streaking nutrient agar with blood drawn under the strictest aseptic precautions from the finger, or from a freshly-killed animal. It may be used in the 'slope' form or as plates. The gonococcus grows favourably on this medium.—N.B.—For Gonococci and Pneumococci use the patient's blood if possible.

**Glucose Agar** consists of nutrient agar to which 1 or 2% glucose has been added after filtration. In the upright form is used also for deep stab cultivations of anaerobic bacteria. Must not be sterilised in the autoclave.

**Glycerin Agar** is nutrient agar with the addition of 5 to 8% of glycerin. Is a satisfactory medium for the growth of *Bacillus diphtheriæ*, *B. tuberculosis* and *Streptothrix actinomycosis*.

**Maltose Agar.**—Maltose 12, Peptone (in powder) 3, Agar 3.9, Water 300. This is prepared in the customary manner, but the product is not neutralised. Blaxall's formula is Maltose 12, Peptone 1½, Agar 9, Water 300. For ringworm cultivation.

**Peptone-water.**—Peptone 5 Gm., sodium chloride 10 Gm., tap water 1,000 Cc.; boil in the steamer one hour, filter, and sterilise. Not necessary to render alkaline. Used for the production of the indol reaction as one of the aids, for example, to distinction (?) of *B. typhi abdominalis* and *B. coli*. It was originally utilised for cholera-diagnosis. It is Dunham's solution.

**Potato.**—Large specimens are thoroughly cleaned and cut into 'half-cylinders' with a potato-borer. The brown peel is removed and the pieces soaked overnight in water to wash off excess of starch. Wide test-tubes (1 inch by 6 inches) are plugged and sterilised, and a little distilled water is placed with each half-cylinder in the tubes. The water prevents drying up in sterilising, which is effected by heating on three successive days. Must not be sterilised in the autoclave.

Potatoes prepared as above may be soaked in 5% glycerin water for several hours previous to putting into tubes. These are very useful for the cultivation of the tubercle bacillus.

**Milk.**—The cream is skimmed from good cows' milk, and the resulting 'skimmed' milk sterilised in the steamer for ½ hour on three successive days.

May also be drawn direct by means of a catheter into sterile vessels with the strictest aseptic precaution. Organisms are said to grow better in this than in milk which has been heated.

**Litmus Milk.**—The above—with a small proportion of Litmus solution added. Used for detection of acid formation.

**Blood-serum.**—The serum is separated from fresh blood obtained from the jugular vein of the sheep. It is centrifugalised and filtered through a sterile Chamberland filter. (The candle is heated in a muffle-furnace, or in a bright fire, if it has been previously used for the same purpose). The filtrate may then be poured into sterile test-tubes, plugged—and inspissated, first at

80° C., then at 60° C., and the latter temperature is maintained eight to twelve hours, or more if necessary. The medium is finally tested after capping by incubating at 37° C. for twenty-four hours to ensure sterility.

**Löffler's Blood Serum.**—This consists of ordinary 'Serum' 3 parts mixed with neutral peptone bouillon 1 part with 1% grape sugar added to it. Tubes are filled and sterilised as under Blood Serum.

**Elschnig's Medium** is a fluid one in which the utmost reliance is placed for detecting pneumococci. It consists of 1 part of Horse Serum and 3 parts of bouillon without Peptone.—*Glas. Med. Jl.*, Feb. 1913.

## EMBALMING.

If it is impossible to make the autopsy at once, preservative may be injected into the body until such time as convenient; about 300 Cc. of 5% solution of **Formalin** suffice. It is introduced through the arteries (arterial embalming) or a coarse trocar and cannula may be driven deeply into the tissue and the cavities and organs injected (cavity embalming).

**Perchloride Embalming.**—The former method is usually practised by opening one of the large superficial arteries, as the femoral, and forcing the fluid through the vessels. Nauwerck uses the following—500 Cc. injection syringe; long cannulæ of different calibres, with pear shaped ends and wit stopcocks or, preferably, with double stopcocks; strong twine; scalpels, scissors, forceps, grooved director, hæmostats, an aneurism-needle, and ordinary needles; basins and buckets; several packages of absorbent cotton; cloths and sponges; and 10 litres of a 10% solution of mercuric chloride. His method of embalming is begun by exposing the lower part of the abdominal aorta and the two iliac arteries. Two ligatures are placed beneath the aorta about two finger-breadths apart, and the aorta is obliquely incised to allow the entrance of the cannula, which is secured by tying the distal ligature over it. The injection into the upper part of the body is then begun carefully and slowly, pausing occasionally when the counter-pressure becomes too great. About 3 litres are injected or less, depending upon the appearance of swelling of the face, seen first about the eyes and chin. The cannula is removed, both proximal and distal ligatures are tied, and the aorta is cut through. In like manner a litre of the solution is injected into each leg through the common iliac artery. A cannula with a double stopcock can be used to inject both the upper and lower parts of the body at the same time. The mesentery is ligatured and the intestines, from the beginning of the jejunum to the end of the sigmoid flexure, are removed; opened, washed out, and put in a 1% solution of mercuric chloride, and later replaced in the abdominal cavity, wrapped in sublimate wool, or where practicable, disposed of by cremation. The stomach, duodenum and rectum are cleaned out with sublimate solution and packed with sublimate wool. The bladder, vagina, external ear, and nose are similarly treated. The abdominal cavity is carefully wiped with a cloth wrung out of the perchloride solution and dried, and the abdominal incision is sewn up. The surface of the body, with the exception of the hair, is also wiped with the solution and dried. If this method fails, Nauwerck injects into the carotid and axillary arteries.

**Formalised Arsenical Embalming Injection.**—Hewson recommends the following injection for embalming—Sodium Arsenate 40, boiling water 157. Boil until dissolved and add glycerin 40, formalin 2 or 3. About 2 and one-half gallons are introduced into an artery—say the common carotid—by gravity, openings having been previously made in the toes or in several of the veins if they be distended with blood. After the injection the body is thoroughly greased, covered with paper, bandaged and placed in cold storage until wanted for dissection. *Caution.*—These solutions are caustic in action on the hands.—*Cattell's Post-Mortem Pathology*.



# INTERNATIONAL, 1915, ATOMIC WEIGHTS.

The Molecular Weights of Compounds in our work are now given throughout in terms of the International, 1915, Atomic Wts.

		I. Wts. O = 16.
Aluminium	Al	27.1
Antimony	Sb	120.2
Argon	A	39.88
Arsenic	As	74.96
Barium	Ba	137.37
Bismuth	Bi	208.0
Boron	B	11
Bromine	Br	79.92
Cadmium	Cd	112.4
Cæsium	Cs	132.81
Calcium	Ca	40.07
Carbon	C	12.00
Cerium	Ce	140.25
Chlorine	Cl	35.46
Chromium	Cr	52.0
Cobalt	Co	58.97
Columbium	Cb	93.5
Copper	Cu	63.57
Dysprosium	Dy	162.5
Erbium	E	167.7
Europium	Eu	152.0
Fluorine	F	19
Gadolinium	Gd	157.3
Gallium	Ga	69.9
Germanium	Ge	72.5
Glucinum	Gl	9.1
Gold	Au	197.2
Helium	He	3.99
Holmium	Ho	163.5
Hydrogen	H	1.008
Indium	In	114.8
Iodine	I	126.92
Iridium	Ir	193.1
Iron	Fe	55.84
Krypton	Kr	82.92
Lanthanum	La	139.0
Lead	Pb	207.1
Lithium	Li	6.94
Lutecium	Lu	174
Magnesium	Mg	24.32
Manganese	Mn	54.93
Mercury	Hg	200.6

		I. Wts. O = 16.
Molybdenum	Mo	96.0
Neodymium	Nd	144.3
Neon	N	20.2
Nickel	Ni	58.68
Niton (Ra Emanation)	Nt	222.4
Nitrogen	N	14.01
Osmium	Os	190.9
Oxygen	O	16.00
Palladium	Pd	106.7
Phosphorus	P	31.04
Platinum	Pt	195.2
Potassium	K	39.1
Praseodymium	Pr	140.6
Radium	Ra	226.4
Rhodium	Rh	102.9
Rubidium	Rb	85.45
Ruthenium	Ru	101.7
Samarium	Sa	150.4
Scandium	Sc	44.1
Selenium	Se	79.2
Silicon	Si	28.3
Silver	Ag	107.88
Sodium	Na	23
Strontium	Sr	87.63
Sulphur	S	32.07
Tantalum	Ta	181.5
Tellurium	Te	127.5
Terbium	Tb	159.2
Thallium	Tl	204
Thorium	Th	232.4
Thulium	Tm	168.5
Tin	Sn	119.0
Titanium	Ti	48.1
Tungsten	W	184.0
Uranium	U	238.5
Vanadium	V	51
Xenon	X	130.2
Ytterbium	Yb	172.0
Yttrium	Yt	89.0
Zinc	Zn	65.37
Zirconium	Zr	90.6

## Suggested International Atomic Weights for Pharmaceutical Purposes.

(From a paper by W.H.M., read at an Evening Meeting of the Pharmaceutical Society of Great Britain, in London. P. J. i./II, 170,178).

The atomic weights of elements employed in the pharmacopœias of different nations show variation in magnitude, particularly with regard to the first, second and third place of decimals. The important elements arsenic, bismuth, bromine, chlorine, iodine, lithium, silver, sodium, all show variations, and these are not accounted for by the fact that the oxygen standard is adopted by some and the hydrogen standard by others. The International Committee on Atomic Weights every year\* introduces corrections, necessary scientifically from time to time; for example, the Committee of 1909 introduced corrections in chlorine, sulphur, iodine, magnesium, and sodium. In 1910 arsenic and chromium were altered. In 1911 lithium, phosphorus, platinum, and strontium (*inter alia*) were altered. In 1912 calcium, iron, mercury and thorium were amongst those altered. The author suggests the following 'Rounded off' weights which are those in the French Pharmacopœia, with the exception of a slight alteration of Platinum and the addition of Cerium, Thorium and Tin, as sufficiently accurate for general pharmaceutical work. If "rounded-off" International Standards for Pharmaceutical Purposes could be arranged, they would tend to general uniformity. These pharmaceutical standards should, it is suggested, be officially adopted in the pharmacopœias in different countries on their next revisions, and should remain in force for some years, or until some important discovery necessitated a complete radical change in one or more of the weights. It is obviously unsatisfactory for a pharmacopœia of any nation to adopt International Weights issued by the Committee thereon as is the custom, because these are continually fluctuating—particularly in view of the fact that a pharmacopœia is usually current as a standard work for a period of ten years or thereabouts. The pharmacist, however, in carrying out his pharmaceutical operations is able to control his products without the necessity of employing ultra-scientific figures. The author has not lost sight of the fact that analytical data would be influenced by a "rounded-off" revision. The influence on the whole would be for the general good. Again, an International Unification for pharmacy as suggested would do away with the extraordinary anomaly of seven current European pharmacopœias giving one of the most important elements four different weights, and only two of the four agreeing with the current "International Atomic Weights."

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\* It is satisfactory to note that no further changes will be introduced during 1915.



## SUGGESTED ATOMIC WEIGHTS.

Aluminium .....	27	Lithium .....	7
Antimony .....	120	Magnesium .....	25
Arsenic .....	75	Manganese .....	54
Barium .....	137	Mercury .....	204
Bismuth .....	208	Nitrogen .....	50
Boron .....	11	Oxygen .....	23
Bromine .....	80	Phosphorus .....	61
Calcium.....	40	Platinum .....	139
Carbon .....	12	Potassium.....	12
Cerium .....	140	Silicon .....	91
Chlorine .....	35.5	Silver.....	135
Chromium .....	52	Sodium .....	29
Copper .....	63.5	Strontium .....	08
Gold .....	197	Sulphur .....	28
Hydrogen .....	1	Tin.....	183
Iodine .....	127	Zinc .....	37
Iron .....	56	Thorium .....	261
Lead .....	207		

A Note on Percentage errors with "Rounded off" weights—P.J. i./12, 365.

ATOMIC WEIGHTS, DETERMINATIONS OF.—An eulogy of work in America. Of the 83 elements at present known and of which the atomic weights are given annually in the International Tables, 28 of these estimations, which are regarded as among the best ascertained values, are to be credited to the Harvard laboratory.—Nature, Aug. 18, 1910, p. 207.

Periodic Table of Elements founded on that of Mendeléeff. Revised to 1915 Atomic Weights.

Zero Group.	Group I.	Group II.	Group III.	Group IV.	Group V.	Group VI.	Group VII.	Group VIII.
<i>x</i>								
<i>y</i>	H=1.008							
He=3.99	Li=6.94	Gl(Be)=9.1	B=11	C=12	N=14.01	O=16	F=19	
Ne=20.2	Na=23	Mg=24.32	Al=27.1	Si=28.3	P=31.04	S=32.07	Cl=35.46	
A=39.88	K=39.1	Ca=40.07	Sc=44.1	Ti=48.1	V=51	Cr=52	Mn=54.93	Fe=55.84 Co=58.97 Ni=58.68
	Cu=63.57	Zn=65.37	Ga=69.9	Ge=72.5	As=74.96	Se=79.2	Br=79.92	
Kr=82.92	Rb=85.45	Sr=87.63	Yt=89	Zr=90.6	Cb=93.5	Mo=96		Ru=101.7 Rh=102.9 Pd=106.7
	Ag=107.88	Cd=112.4	In=114.8	Sn=119	Sb=120.2	Te=127.5	I=126.92	
Xe=130.2	Cs=132.81	Ba=137.37	La=139	Ce=140.25				
			Yb=172		Ta=181.5	W=184		Os=190.9 Ir=193.1 Pt=195.2
	Au=197.2	Hg=200.6	Tl=204	Pb=207.1	Bi=208			
		Ra=226.4		Th=232.4		U=238.5		

In an Appendix to "The Principles of Chemistry, 1905," Mendeléeff included the elements of the Argon group and Radium, and found places in addition for two hypothetical elements which he placed before Helium and designated *x* and *y*. *y* is supposed to be an analogue of Helium and may be identified hereafter with "Coronium" which has been recognised in the Sun's coronal atmosphere. This gas according to Mendeléeff would have density about 0.2 and therefore, molecular weight 0.4 or about  $\frac{1}{16}$  that of Helium.

*x* is the 'Ether' for which Mendeléeff supposes a molecular structure. It is assumed to be inert like the Argon group and to possess a low density and Atomic Weight estimated at 0.000,000,000,053.—Mendeléeff Memorial Lecture.—Tilden, "Nature," 3/2/10, p. 416.

An element with the atomic weight 3 has been found by J. J. Thomson—? some allotropic variety of Hydrogen analogous with Ozone and Oxygen. An element with this weight had been predicted by Mendeléeff, who endowed it with super-fluorine properties.—P.J. i./13, 101.



# ACTION OF ACIDS ON THE COMMON METALS AND THEIR OXIDES.

The reaction between Acids and the Common Metals is a matter frequently arising and one concerning which information is not always available. In arranging the following table it was necessary to check many of the interactions experimentally as we found statements in the literature to vary greatly in many instances.

SUBSTANCE.	Acid HYDROCHLORIC. Conc. Sp. gr. 1.16.*	Dilute. Sp. gr. 1.052.†	ACID SULPHURIC. Conc. Sp. gr. 1.843.†	Dilute.‡ Sp. gr. 1.094.	ACID NITRIC. Conc.* Sp. gr. 1.42.	Dilute.‡ Sp. gr. 1.101.	REMARKS.
§ <b>Aluminium</b>	Hot. Soluble. Forms $\text{AlCl}_3$ .	Easily Soluble. — forms $\text{AlCl}_3$ .	Soluble. Forms $\text{Al}_2(\text{SO}_4)_3$	Slowly attacked.	Soluble. Forms $\text{Al}(\text{NO}_3)_3$ and Oxides of Nitrogen.	Slowly soluble.	Attacked by NaOH or KOH Solutions. Soluble in cold Acetic Acid, quicker in hot.
	Cold. Ditto.	Ditto.	Slightly attacked. Slightly soluble.	Unattacked	Scarcely attacked.	No action.	
	Hot. Slightly Soluble. (Forms $\text{AlCl}_3$ ).	Slowly soluble. (Forms $\text{AlCl}_3$ ).	Slightly soluble.	Soluble. Forms $\text{Al}_2(\text{SO}_4)_3$	Slowly soluble.	Slowly soluble.	<i>Ignited</i> (Amorphous) Oxide is unattacked by Acids, except hot $\text{H}_2\text{SO}_4$ .
	Cold. Almost insoluble.	Ditto.	Ditto.	ditto.	Forms $\text{Al}(\text{NO}_3)_3$ . Ditto.	Ditto.	
<b>Antimony</b>	Hot. Pure Antimony is insoluble.	Slightly soluble.	Soluble. Forms $\text{Sb}_2(\text{SO}_4)_3$ and $\text{SO}_2$	Insoluble.	Oxidised but not dissolved.	Oxidised but not dissolved.	Aqua Regia dissolves forming Antimonious or Antimonious Chloride according to duration of action
	Cold. No action.	No action.	No action.	Insoluble.	Practically no action.	No action.	
<b>Antimonic Oxide.</b> $\text{Sb}_2\text{O}_5$ .	Hot. (Forms $\text{SbCl}_5$ ).	Slightly soluble.	Soluble.	Slightly soluble.	Practically insoluble.	Very slightly soluble.	
	Cold. Slowly soluble to form $\text{SbCl}_5$ .	No action.	Slightly soluble.	Very slightly soluble.	Ditto.	Ditto.	Soluble in KOH and NaOH Solutions Insoluble in $\text{NH}_4\text{OH}$ .

\* = Off.

† = Off. approx.

‡ = B.P.'98.

§ See under Chromium.

SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16.	ACID SULPHURIC. Conc. Sp. gr. 1.843.	ACID NITRIC. Conc. Sp. gr. 1.42.	REMARKS.
<b>Antimonous Oxide</b> $\text{Sb}_2\text{O}_3$	Hot. Soluble. Forms $\text{SbCl}_3$ .	Soluble.	Forms $\text{Sb}_2\text{O}_5$ and $\text{Sb}_4\text{O}_6$ .	Soluble in Acetic, Tartaric and Benzoic Acids, also in Glycerin, Sodium Hydrate and Potassium Hydrate Solutions.
	Cold. Slowly soluble.	Slightly soluble.	Slightly soluble.	Easily soluble in Aqua Regia forming $\text{SbCl}_3$ or $\text{SbCl}_5$ according to length of action.
<b>Arsenium</b>	Hot. Slowly soluble. Forms $\text{AsCl}_3$ .	Soluble. Forms $\text{As}_2\text{O}_3$ and $\text{SO}_2$ .	Soluble. Forms $\text{H}_3\text{AsO}_4$ .	Soluble in Sodium Hypochlorite Solution.
	Cold. Practically no action.	No action.	Practically no action.	Very soluble in water
<b>Arsenic Oxide</b> $\text{As}_2\text{O}_5$	Hot. Soluble. Forms $\text{AsCl}_3$ and Chlorine on prolonged boiling.	Soluble.	Soluble.	
	Cold. Soluble with- out change.	Ditto.	Ditto.	
<b>Arsenious Oxide</b> $\text{As}_2\text{O}_3$	Hot. Soluble. Forms $\text{AsCl}_3$ .	Slightly soluble.	Soluble. Forms $\text{H}_3\text{AsO}_4$ .	Soluble in Alkalies.
	Cold. Ditto.	Slowly soluble.	Ditto.	Slightly soluble, without changing.



SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16.	ACID SULPHURIC. Conc. Dilute. Sp. gr. 1.843. Sp. gr. 1.094.	ACID NITRIC. Conc. Dilute. Sp. gr. 1.42. Sp. gr. 1.101.	REMARKS.
<b>Bismuth</b>	Hot. Scarcely acted on.	A slightly soluble basic Sulphate formed and $\text{SO}_2$ .	Soluble. Forms Bi $(\text{NO}_3)_3$ and oxides of Nitrogen.	Aqua Regia converts into Bi $\text{Cl}_3$ .
	Cold. Insoluble.	Scarcely acted on. Schmidt says forms Bi $(\text{SO}_4)_3$ .	Ditto.	
	Hot. Soluble. Forms Bi $\text{Cl}_3$ .	Slightly soluble. Forms Bi $(\text{SO}_4)_3$ . Very slightly soluble. Easily soluble.	Soluble. Forms Bi $(\text{NO}_3)_3$ .	Soluble in strong hot NaOH Solution.
<b>Chromium</b> (Reduced from $\text{CrCl}_3$ by Zn.)	Cold. Ditto.	Forms Bi $(\text{SO}_4)_3$ . Very slightly soluble. Easily soluble.	Ditto.	
	Hot. Soluble. Forms $\text{CrCl}_2$ quickly oxidizing to $\text{CrCl}_3$ .	Forms $\text{CrSO}_4$ quickly oxidizing to $\text{Cr}_2(\text{SO}_4)_3$ .	Practically no action.	' $\beta$ ' Chromium reduced from $\text{CrCl}_3$ by ignition with Carbon is said to be unattacked by Aq. Regia or any Acids.
	Cold. Ditto.	Insoluble.	Insoluble.	
<b>Chromic Oxide</b> $\text{Cr}_2\text{O}_3$ (Green Amorphous.)	Hot. Soluble. Forms $\text{CrCl}_3$ .	Forms $\text{Cr}_2(\text{SO}_4)_3$ .	Soluble. Forms Cr $(\text{NO}_3)_3$ (?).	Crystalline $\text{Cr}_2\text{O}_3$ is insoluble in all Acids
	Cold. Ditto.	Ditto.	Ditto.	

\*NOTE.—By dissolving strongly heated Chromic Oxide in hot concentrated  $\text{HNO}_3$  (1.4) a solution is obtained from which  $\text{Cr}_2(\text{NO}_3)_6 \cdot 15\text{H}_2\text{O}$  crystallises on cooling. In dry air this loses  $6\text{H}_2\text{O}$  with formation of  $\text{Cr}_2(\text{NO}_3)_4 \cdot 9\text{H}_2\text{O}$ . Similarly  $\text{Al}_2(\text{NO}_3)_6 \cdot 15\text{H}_2\text{O}$  is produced stable in ordinary air.—Milorad Z. Jovitschitsch Monatsch, 1912, 33, 9-18 per J. C. S. A. ii. 12, 261.

SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16.	ACID SULPHURIC. Conc. Sp. gr. 1.843.	ACID NITRIC. Conc. Sp. gr. 1.42.	REMARKS.
<b>Chromic Oxide</b> $\text{CrO}_3$ (Red).	Hot. Soluble. Forms $\text{CrCl}_3$ and Chlorine. Soluble with- out decom- position un- less the sol- ution be very con- centrated.	Soluble. Forms $\text{Cr}_2(\text{SO}_4)_3$ and Oxygen.	Soluble with- out decom- position.	Very soluble in water to form $\text{H}_2\text{CrO}_4$ .
	Cold. Ditto.	Ditto.	Ditto.	
	Hot. Soluble. Forms $\text{CoCl}_2$	Attacked. Forms $\text{Co}(\text{SO}_4)$ and $\text{SO}_2$ .	Soluble. Forms $\text{Co}(\text{NO}_3)_2$ and Nitro- gen Oxides. Ditto.	
	Cold. Ditto.	Unattacked. Ditto.	Ditto.	
<b>Cobalt (ous) Oxide</b>	Hot. Soluble. Forms $\text{CoCl}_2$ .	Soluble. Forms $\text{Co}(\text{SO}_4)$ .	Soluble. Forms $\text{Co}(\text{NO}_3)_2$ .	
	Cold. Ditto.	Ditto.	Ditto.	
	Hot. Soluble. Forms $\text{CoCl}_2$ .	Soluble. Forms $\text{Co}(\text{SO}_4)$ .	Soluble. Forms $\text{Co}(\text{NO}_3)_2$ .	
<b>Copper</b>	Hot. Very slowly soluble. Forms $\text{CuCl}_2$ (in con- tact with the air).	Slowly sol- ible. Forms $\text{CuSO}_4$ and $\text{SO}_2$ .	Soluble. Forms $\text{Cu}(\text{NO}_3)_2$ and Oxides of Nitrogen.	Slowly soluble in Con- centrated Solutions of Caustic Alkalies.
	Cold. Not attacked.	Not attacked.	Ditto.	Scarcely attacked.



SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16, Dilute. Sp. gr. 1.052.		ACID SULPHURIC. Conc. Sp. gr. 1.843. Dilute. Sp. gr. 1.094.		ACID NITRIC. Conc. Sp. gr. 1.42. Dilute. Sp. gr. 1.101.		REMARKS.
Copper (-ic) Oxide (Black) CuO	Hot.	Soluble. Forms CuCl <sub>2</sub> .	Soluble. Forms CuSO <sub>4</sub> .	Soluble. Forms CuSO <sub>4</sub> .	Soluble. Forms Cu(NO <sub>3</sub> ) <sub>2</sub> .	Soluble. Forms Cu(NO <sub>3</sub> ) <sub>2</sub> .	Slowly soluble in hot concentrated caustic alkali Solutions.
	Cold.	Ditto.	Slightly soluble.	Ditto.	Ditto.	Ditto.	
Copper (ous) Oxide (Red) Cu <sub>2</sub> O.	Hot.	Soluble. Forms Cu <sub>2</sub> Cl <sub>2</sub> .	Soluble. Forms CuSO <sub>4</sub> and SO <sub>2</sub> .	Forms CuSO <sub>4</sub> and Copper.	Soluble. Forms Cu(NO <sub>3</sub> ) <sub>2</sub> and Oxides of Nitrogen.	Soluble. Forms Cu(NO <sub>3</sub> ) <sub>2</sub> and Oxides of Nitrogen. Slightly soluble.	Same as Black Oxide.
	Cold.	Forms Cu Cl <sub>2</sub> and Copper.	Forms CuSO <sub>4</sub> and Copper.	Ditto.			
Gold	Hot.	Not attacked.	Not attacked.	Not attacked.	Not attacked.	Not attacked.	Soluble in Aqua Regia to form AuCl <sub>3</sub> .
	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
Gold (ic) Oxide. Au <sub>2</sub> O <sub>3</sub> .	Hot.	Slightly soluble.	Slightly soluble.	Slightly soluble.	Soluble.	Slightly soluble.	Soluble in Conc. KOH Solution and KCN Solution.
	Cold.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
Iron.	Hot.	Soluble. Forms FeCl <sub>2</sub> . FeCl <sub>3</sub> .	Soluble. Forms Fe SO <sub>4</sub> and SO <sub>2</sub> .	Soluble. Forms Fe SO <sub>4</sub> .	Soluble. Forms Fe (NO <sub>3</sub> ) <sub>3</sub> and Oxides of Nitrogen.	Soluble. Forms Fe (NO <sub>3</sub> ) <sub>3</sub> and Oxides of Nitrogen.	
	Cold.	Ditto.	No action.	Ditto.	Rendered passive.	Ditto.	

SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16.	ACID SULPHURIC. Conc. Sp. gr. 1.843.	ACID NITRIC. Conc. Sp. gr. 1.42.	REMARKS.
Iron (-ic) Oxide. $\text{Fe}_2\text{O}_3$ .	Hot. Soluble. Forms $\text{Fe}_2\text{Cl}_6$ .	Forms $\text{Fe}_2(\text{SO}_4)_3$ which dis- solves on dilution. Action slight.	Very slight action.	Strongly ignited Ox- ide practically in- soluble in all acids.
	Cold. Action slight.	Action slight.	Practically no action.	
	Hot. Action slight. Forms $\text{PbCl}_2$ .	Action very vigorous. Forms $\text{PbSO}_4$ .	Action slow. Forms $\text{Pb}(\text{NO}_3)_2$ & oxides of Nitrogen. Action slight.	Action greatly de- pends on the con- dition of the lead— whether sheet or finely divided, etc.
Lead.  Lead Oxide (Litharge) $\text{PbO}$ .	Cold. Action very slight.	Action very slight.	Action slight.	
	Hot. Soluble. Forms $\text{PbCl}_2$ .	Forms $\text{PbSO}_4$ .	Readily sol- uble. Forms $\text{Pb}(\text{NO}_3)_2$ . Ditto. Soluble. Forms $\text{Mg}(\text{NO}_3)_2$ Oxides of Nitrogen, Hydrogen and Am- mon. Ni- trate. Ditto.	Soluble in conc. KOH and NaOH solu- tions. Easily in Acetic Acid.
Magnesium	Cold. Ditto.	Ditto. Soluble. Forms $\text{MgSO}_4$ $\text{MgH}_2(\text{SO}_4)_2$ and $\text{SO}_2$ .	Ditto. Soluble. Forms $\text{Mg}(\text{NO}_3)_2$ Hydrogen & Oxides of Nitrogen.	Soluble in Ammon- ium Chloride Solu- tion.
	Hot. Easily sol- uble. Forms $\text{MgCl}_2$ .	Ditto. Easily sol- formable. $\text{MgCl}_2$ .	Ditto.	
	Cold. Ditto.	Action very slight.	Ditto.	



SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16,	ACID SULPHURIC. Conc. Sp. gr. 1.843.	ACID NITRIC. Dilute. Sp. gr. 1.101.	REMARKS.
Magnesium Oxide. MgO.	Hot. Readily sol- uble. Forms MgCl <sub>2</sub> .	Readily sol- uble. Forms Mg SO <sub>4</sub> & MgH <sub>2</sub> (SO <sub>4</sub> ) <sub>2</sub> .	Readily sol- uble. Forms Mg(NO <sub>3</sub> ) <sub>2</sub> .	Soluble in Ammon- ium Salts, also in Organic Acids.
	Cold. Ditto.	Ditto.	Ditto.	
Manganese	Hot. Easily sol- uble. Forms MnCl <sub>2</sub> .	Soluble. Forms Mn SO <sub>4</sub> and SO <sub>2</sub> .	Easily sol- uble. Forms Mn(NO <sub>3</sub> ) <sub>2</sub> & Mn(NO <sub>3</sub> ) <sub>2</sub> & Oxides of Nitrogen. Ditto.	
	Cold. Ditto.	Action slight.	Ditto.	
Manganese Dioxide MnO <sub>2</sub> .	Hot. Soluble. Forms MnCl <sub>2</sub> and Chlorine.	Action slight. Forms MnSO <sub>4</sub> and Oxygen at 200° C. [or Mn <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> at 100° C.] —Schmidt.	Action very slight.	MnO <sub>2</sub> is more sol- uble in diluted Sul- phuric Acid in presence of easily oxidisable bodies (FeSO <sub>4</sub> , Sugar etc). with formation of MnSO <sub>4</sub> and O., the O then oxidises the substances in question.
	Cold. Ditto.	Practically no action.	No action.	

SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16.	ACID HYDROCHLORIC. Dilute. Sp. gr. 1.052.	ACID SULPHURIC. Conc. Sp. gr. 1.843.	ACID SULPHURIC. Dilute. Sp. gr. 1.094.	ACID NITRIC. Conc. Sp. gr. 1.42.	ACID NITRIC. Dilute Sp. gr. 1.101.	REMARKS.
<b>Mercury</b>	Hot. No action.	No action.	Forms HgSO <sub>4</sub> , SO <sub>2</sub> and Hg <sub>2</sub> SO <sub>4</sub> according to proportions and temperature.) No action.	Practically no action.	Soluble. Forms Hg(NO <sub>3</sub> ) <sub>2</sub> & Oxides of Nitrogen.	Soluble. Forms Hg(NO <sub>3</sub> ) <sub>2</sub> & Oxides of Nitrogen.	
	Cold. Ditto.	Ditto.	No action.	Ditto.	Soluble. Forms Hg(NO <sub>3</sub> ) <sub>2</sub> & some Hg <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> and Oxides of Nitrogen.	Very slightly soluble. Forms Hg <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub>	
	Hot. Soluble. Forms HgCl <sub>2</sub> .	Soluble. Forms HgCl <sub>2</sub> .	Soluble. Forms HgSO <sub>4</sub> .	Soluble. Forms HgSO <sub>4</sub> .	Soluble. Forms Hg(NO <sub>3</sub> ) <sub>2</sub> .	Soluble. Forms Hg(NO <sub>3</sub> ) <sub>2</sub> .	Combines easily with Organic Acids when freshly precipitated.
<b>Nickel</b>	Cold. Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
	Hot. Soluble. Forms NiCl <sub>2</sub> .	Very slowly soluble. Forms NiCl <sub>2</sub> .	Action slight. Forms Ni SO <sub>4</sub> and SO <sub>2</sub> .	Very slowly soluble. Forms NiSO <sub>4</sub> .	Easily soluble. Forms Ni (NO <sub>3</sub> ) <sub>2</sub> and Oxides of Nitrogen.	Easily soluble. Forms Ni (NO <sub>3</sub> ) <sub>2</sub> and Oxides of Nitrogen.	
	Cold. Ditto.	Ditto.	Practically no action.	Ditto.	Rendered passive.	Ditto.	
<b>Nickel</b> (-ous) Oxide NiO.	Hot. Soluble. Forms NiCl <sub>2</sub> .	Soluble. Forms NiCl <sub>2</sub> .	Forms NiSO <sub>4</sub> .	Soluble. Forms NiSO <sub>4</sub> .	Soluble Forms Ni(NO <sub>3</sub> ) <sub>2</sub> .	Soluble. Forms Ni(NO <sub>3</sub> ) <sub>2</sub> .	Soluble in NH <sub>4</sub> OH.
	Cold. Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	



SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16.	ACID HYDROCHLORIC. Dilute. Sp. gr. 1.052.	ACID SULPHURIC. Conc. Sp. gr. 1.843.	ACID SULPHURIC. Dilute. Sp. gr. 1.094.	ACID NITRIC. Conc. Sp. gr. 1.42.	ACID NITRIC. Dilute. Sp. gr. 1.101.	REMARKS.
<b>Nickel (-ic) Oxide Ni<sub>2</sub>O<sub>3</sub>.</b>	Hot. Soluble. Forms Ni Cl <sub>2</sub> and Oxygen.	Soluble. Forms Ni Cl <sub>2</sub> and Oxygen.	Forms NiSO <sub>4</sub> .	Soluble. Forms Ni SO <sub>4</sub> and Oxygen.	Soluble. Forms Ni (NO <sub>3</sub> ) <sub>2</sub> and Oxygen.	Soluble. Forms Ni (NO <sub>3</sub> ) <sub>2</sub> and Oxygen.	Soluble in NH <sub>4</sub> OH c evolution of Nitro- gen.
	Cold. Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	
<b>Platinum</b>	Hot. No action.	No action.	No action.	No action.	No action.	No action.	Soluble in Aqua Regia to form PtCl <sub>4</sub> .
	Cold. Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	Ditto.	Finely divided Sil- ver is more respon- sive than compact Silver to Hydro- chloric Acid.
<b>Silver Oxide</b>	Hot. Practically no action.	Practically no action.	Soluble. Forms Ag <sub>2</sub> SO <sub>4</sub> and SO <sub>2</sub> .	Action very slight.	Soluble. Forms Ag NO <sub>3</sub> and Oxides of Nitrogen.	Soluble. Forms Ag NO <sub>3</sub> and Oxides of Nitrogen.	Soluble in N <sub>4</sub> OH and KCy Solutions.
	Cold. Ditto.	Ditto.	No action.	No action.	Ditto.	Ditto.	
<b>Tin</b>	Hot. Forms AgCl.	Forms AgCl.	Soluble. Forms Ag <sub>2</sub> SO <sub>4</sub> .	Soluble. Forms Ag <sub>2</sub> SO <sub>4</sub> .	Soluble. Forms AgNO <sub>3</sub> .	Soluble. Forms AgNO <sub>3</sub> .	
	Cold. Ditto.	Ditto.	Ditto.	Slightly soluble.	Ditto.	Ditto.	
<b>Tin</b>	Hot. Soluble. Forms SnCl <sub>2</sub> .	Soluble. Forms SnCl <sub>2</sub> .	Dissolves forming Sn SO <sub>4</sub> (Stan- nous Sul- phate) SO <sub>2</sub> and Sul- phur.	Slowly sol- uble. Forms SnSO <sub>4</sub> .	Forms H <sub>2</sub> SnO <sub>3</sub> (Meta- stannic Acid) Ox- ides of Nit- rogen and NH <sub>4</sub> NO <sub>3</sub> .	Soluble. Forms SnO <sub>3</sub> , Sn (NO <sub>3</sub> ) <sub>4</sub> and Oxides of Nit- rogen and NH <sub>4</sub> NO <sub>3</sub> .	Soluble in hot Con- centrated NaOH or KOH solution. Forms Stannates K <sub>2</sub> SnO <sub>3</sub> or Na <sub>2</sub> SnO <sub>3</sub> .
	Cold. Soluble. Forms SnCl <sub>2</sub> .	Practically no action.	Action slight.	Practically no action.	Ditto.	Soluble. Forms Sn(NO <sub>3</sub> ) <sub>2</sub> NH <sub>4</sub> NO <sub>3</sub> and very little gas.	Aqua Regia in excess dissolves to form Stannic Chloride SnCl <sub>4</sub> .

SUBSTANCE.	ACID HYDROCHLORIC. Conc. Sp. gr. 1.16.	ACID SULPHURIC. Conc. Sp. gr. 1.843.	ACID NITRIC. Conc. Sp. gr. 1.42.	REMARKS.
Tin (-ic) Oxide $\text{SnO}_2$ .	Hot. No action.	Slightly soluble.	No action.	Slightly soluble in hot conc. NaOH or KOH solutions
	Cold. Ditto.	No action.	Ditto.	
Tin (-ous) Oxide	Hot. Soluble. Forms $\text{SnCl}_2$ .	Forms $\text{SnO}_4$ . Soluble. Forms $\text{SnSO}_4$ .	Forms $\text{SnO}_2$ and Oxides of Nitrogen. Soluble. Forms $\text{Sn(NO}_3)_2$ .	Newth says solution in NaOH is known as Sodium Staunite
	Cold. Ditto.	Ditto.	Ditto.	
Zinc	Hot. Soluble. Forms $\text{ZnCl}_2$ .	Forms $\text{ZnSO}_4$ & $\text{SO}_2$ .	Soluble. Forms $\text{Zn(NO}_3)_2$ . Oxides of Nitrogen and $\text{NH}_4\text{NO}_3$ .	Soluble in hot Concentrated KOH and NaOH Solutions.
	Cold. Ditto.	Forms $\text{ZnSO}_4$ .	Soluble.	
Zinc Oxide	Hot. Soluble. Forms $\text{ZnCl}_2$ .	Slightly soluble. Forms $\text{ZnSO}_4$ .	Soluble. Forms $\text{Zn(NO}_3)_2$ .	Soluble in $\text{NH}_4\text{Cl}$ NaOH and KOH Solutions.
	Cold. Ditto.	Ditto.	Ditto.	



## CHART FOR THE RECOGNITION OF ORGANIC CHEMICAL BODIES USED IN THERAPEUTICS.

The following chart is intended to assist in the recognition of a number of organic chemicals, both natural and synthetic, used therapeutically. It frequently happens that the Analyst is called upon to identify such substances, and without some aid to guide him the search is sometimes extremely difficult. In working with the chart the tests should be taken in rotation commencing with the action of Heat, afterwards with Heat with Sodium Hydrate, and so on from left to right. It will be found that by a simple process of elimination, bodies can be identified with some degree of accuracy.

The data in the chart have practically all been obtained by personal trials in the author's laboratory. It is possible that in some instances reactions found by others may differ from results here recorded. This may be due to (a) difference in commercial variety, (b) mode of conducting the test. The following notes show methods of procedure adopted:—

HEAT 0.1 Gm. in a 3 by  $\frac{1}{2}$  inch test tube in a Bunsen flame.

HEAT WITH SODIUM HYDRATE.—0.1 Gm. of the substance with about five times its weight of crushed Sodium Hydrate, mixed in tube and heated.

SULPHURIC ACID IN THE COLD.—A portion of the substance on a white tile touched with a glass rod dipped in Concentrated Sulphuric Acid.

SULPHURIC ACID HOT.—0.1 Gm. approx. of the substance placed in test tube, 1 Cc. approx. of Sulphuric Acid added and the mixture heated in Bunsen flame.

NITRIC ACID.—A portion of the substance on a white tile touched with a glass rod dipped in Nitric Acid. Sp. gr. 1.42.

NITROGEN, PHOSPHORUS, SULPHUR and Halogens tested for in usual manner.

SP. GR. and SOLUBILITIES.—In the case of the important substances these are repeated from the body of the "Extra Pharmacopœia." In other cases solubilities have been determined by customary methods.

FERRIC CHLORIDE.—Add a drop or two of Ferric Chloride Test (5%) Solution to about 1 Cc. of 1 in 25 solution in water.

NOTE.—Ferric Chloride with water alone gives brownish color on boiling. In case of a substance, *e.g.*, *Acetanilide* (which does not

color in the cold) giving this also we record the result as 'nil.' (The word 'Nil' throughout the Chart indicates no marked characteristic reaction in a few minutes.)

For the BROMINE WATER TEST, FEHLING'S SOLUTION, MAYER'S TEST, GOLD CHLORIDE TEST, PICRIC ACID TEST, and DRAGENDORFF'S TEST, the 1 in 25 solution of the substance is also used, or, if not soluble to that extent, a saturated solution is employed.

For formulæ for preparation of Fehling's, Mayer's, and Dragendorff's Solutions, *vide* pp. 238, 69, 36.

Gold Chloride Solution is used 1 in 20.

Other **Alkaloidal Reagents** are the following :—

**Ammonium ulpho-molybdate.**—Froehde's Reagent.—Ammonium Molybdate 1 Gm. in Concentrated Sulphuric Acid 100 Cc.

**Erdmann's Reagent.**—Mix 6 drops of Nitric Acid (Sp. Gr. 1.25) with water 100 Cc., add 10 drops of this to 20 Cc. of Concentrated Sulphuric Acid.

**Mandelin's Reagent.**—Sulpho-Vanadic Acid.—A 1% solution of Sodium Vanadate in Concentrated Sulphuric Acid.

**Mercuric Chloride Solution.**—1 in 20.

**Platinic Chloride.**—1 in 20.

**Phospho-Tungstic Acid.**—Dissolve Sodium Tungstate 100 and Sodium Phosphate 70 in Water 500, and acidify with Nitric Acid.

**Phospho-Molybdic Acid.**—Sonnenschein's Reagent.—Consists of a solution of Sodium Phosphomolybdate in Nitric Acid, prepared by acidulating a warm solution (50 to 60° C.) of Sodium Phosphate with Nitric Acid, and adding an excess of Ammonium Molybdate Solution. The yellow precipitate is separated, washed with water, acidulated with Nitric Acid and dissolved in a hot solution of Sodium Carbonate (using as little as possible).

The solution is evaporated to dryness and ignited at low red heat till all Ammonium Salts are volatilised, the residue moistened with Nitric Acid and again ignited. The product, consisting of Phosphomolybdate of Sodium, is dissolved in ten times its weight of water, and Nitric Acid (Sp. Gr. 1.42) added until the precipitate at first produced disappears.

**Tannic Acid.**—A Solution of Tannic Acid 1 in Water 8, Alcohol 1 freshly prepared.

**Wagner's Reagent.**—Iodine in Potassium Iodide. Iodine 5, Potassium Iodide 10, Water 100.

(NOTE.—It is important in testing with this Reagent, *e.g.*, in assaying drugs to determine whether sufficiently extracted, to note that water saturated with Ether and then acidulated gives a precipitate of Iodine on adding this reagent. If a precipitate be obtained in this way confirm by adding water,—if it is due to Iodine caused by the Ether it will dissolve again.—*Am. Jl. Ph.*, April '09, 177.)

Apologies are offered for the use of FORMULÆ in place of long chemical names, *e.g.*, HCl. NaOH, etc—these save space and are quicker to read.



Following the Chart are corroborative data with references to Text Books.

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The Therapeutic properties and further details concerning the substances dealt with are given in the body of the work—consult the index.

Contractions used in the Chart :—

a.	=after	mød.	=moderate.
ac.	=acid.	ne	=neutral.
alc.	=alcoholic.	or.	=orange.
alk.	=alkaline.	pp.	=precipitate.
arom.	=aromatic.	part.	=partially.
b.	=before.	quick.	=quickly.
bl.	=black.	res.	=residue.
br.	=brown.	rediss.	=redissolves.
ch.	=chars.	sl.	=slightly.
col.	=color.	s.	=sine (without).
dec'm.	=decomposes.	sus.	=softens.
dk.	=dark.	str.	=strongly.
dist.	=distillate.	sub.	=sublime or sublimate.
Drag.	=Dragendorff.		
eff.	=effervescent.	v.	=very.
gr.	=green.	vap.	=vapor.
inflam.	=inflammable.	vi.	=violet.
insol.	=insoluble.	wh.	=white.
m.	=melt(s).	yell.	=yellow.
misc.	=miscible.		

The ABBREVIATIONS of AUTHORS' NAMES are in general those used in the body of the "Extra Pharmacopœia."

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub> .	N. P. S. & Hal.	M. Pt. (°C)
1	Acetanilide ...	M. sub. vap. burns	Gives off Aniline.	Nil.	Ch. slowly.	Nil.	N.	113°
2	Acetone ...	Evap. c. inflam. vap.	Inflam. vap.	Nil.	Ch. quick.	Sl. br.	Nil.	—
3	Acetophenone	Evaps., does not ch.	Br. c. inflam. vap.	Nil.	Ch.	Nil.	Nil.	20°
4	Acetozone .....	Ch. c. sub. & white res.	Br. c. sl. arom. odor.	Sl. br.	Ch.	Sl. br.	Nil.	See body
5	Acetyl-para- amido-Salol	M. turns yell. and ch. vap. burns	Vi. and gives blue col. up sides of tube.	Nil.	Red vi. slowly	Nil.	N.	180- 185
6	Acid Aceto- Salicyl.	M. c. Acetic odor, ch. vap. burns	Nil.	Nil.	Goes br. not ch.	Nil.	Nil.	135°
7	„ Acetyl- Coumaric (see TYL- MARIN)	—	—	—	—	—	—	—
8	„ Agaric ...	M. c. eff. ch. br. dist. and inflam. vap.	Nil.	Nil.	Froths. ch. quick.	Nil.	Nil.	137
9	„ Cacody- lic	M. ch. Garlic vap. burns c. As. flame	Nil.	Nil.	Does not ch.	Nil.	Nil.	—
10	„ Cam- phoric	M. and sub. c. inflam. vap.	Eff. c. pleas. odor.	Nil.	Eff. inflam. gas, ch.	Nil.	Nil.	186°
11	„ Carbolic (CRYST.)	M. and evaps. c. inflam. vap.	Nil.	Nil.	Dark red-br. not ch.	Br. c. explo- sion.	Nil.	39°
12	„ Cholalic (COLALIN)	Part. m. c. strange odor. Ch. c. alk. inflam. vap.	Br.	Br.	Dark red-br. Ch. quick.	Br. and gummy	N.	Nil.



No.	SP. GR.	SOL. AQ. (1 in)	SOL. ALC. (1 in)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BROM AQ.	FEH- LING, b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC	DRAQ.
1	—	200	4½	Neut.	Nil.	Wh. pp.	Nil.	Nil.	Nil.	Nil.	Br. pp.
2	.7966 (pure)	Misc.	Misc.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
3	1.03 of liq.	V. sl.	Misc.	Neut.	Nil.	Sl. pp. rediss	Nil.	Nil.	Nil.	Nil.	Br. pp.
4	—	Part.	Part.	Mod. ac.	Sl. buff, pp.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
5	—	V. sl.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
6	—	400	1 in 5	Mod. ac,	Nil b. vi. a.	No pp.	Nil.	Nil.	Nil.	Nil.	Nil.
7	—	—	—	—	—	—	—	—	—	—	—
8	—	Insol.	V. sl.	Neut. (alc. ac.)	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
9	—	½	4	Str. ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
10	—	About 200 or more.	Abt 1½	Mod. ac.	Br. pp. a.	Nil.	Re- duces b.	Nil.	Nil.	Nil.	Nil.
11	—	12	0.16	Neut.	Vi. col. b. br.	Wh. pp. rediss	Nil.	Nil.	Bl. pp comes v. slow.	Nil.	Nil.
12	—	Sl.	Abt. 1	Neut.	Nil b. br. pp. a.	V. sl. pp.	Nil.	Nil.	Nil.	Nil.	V. sl. red- br.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO	N.P.S. & Hal.	M. Pt. (°C)
13	Acid Cinnamic	M. wh. sub. & inflam. vap.	Darkens v. slowly; arom. inflam. vap.	Nil.	Yell. green ch. slowly.	Nil.	Nil.	130°
14	„ Citric	M. clear ch. inflam. vap.	Nil.	Nil.	Eff. inflam. vap. & ch.	Nil.	Nil.	135-154°
15	„ Coumaric	M. ch. c inflam. vap.	Yell. eff. then colorless.	Yell.	Ch. slowly.	Yell. & strong eff.	Nil.	200°
16	„ Cresylic	vaps., vap. burns	Separates in 2 layers up. dark & lower light.	Nil.	Ch. quick.	Violent eff.	Nil.	—
17	„ Gallic	Part n & ch. Orange sub. & br. vap. burns	Turns yell.	Darkens sl.	Gradually deep red and then ch.	Br. c. eff.	Nil.	Nil.
18	„ Glycero-phosph	Evaps. Res. effs & ch. vap. burns	Eff.	Nil.	Ch.	Nil.	P.	—
19	„ Hippuric	M. to clear. liq. ch c inflam. & alk. vap.	Alk. vap.	Nil.	Ch. slowly.	Nil.	N.	187°
20	„ Malic	M. c sub.	Froths. Vap. burns.	Nil.	Ch. vap. burns c. blue flame.	Nil.	Nil.	Abt 180°
21	„ Meconic	Ch. c. wh. sub. & vap.	Orange then colorless.	Nil.	Straw col. not ch.	Nil.	Nil.	Nil.
22	„ Nucleinic	Ch. c. odor of burnt feath'rs	Br. c. alk. vap.	Nil.	Ch.	Gelatinises.	N.P.	Nil.
23	„ Oleic	Distilsc sl. residue ch.	Br., and separates from fused soda.	Br.	Deep red br., then ch.	Delicate vi. col.	Nil.	—



No.	SP. Gr.	SOL. Aq. (1 in --).	Sol. Alc. (1 in --).	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil	MA- YER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG
13	—	Sl.	10½	Faint ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
14	—	0.6	1½	Ac.	Nil b. br., pp. a.	Nil.	Nil b. & a.	Minute crys- tals a. a while.	Nil.	Nil.	Nil.
15	—	600	12 (or less).	Sl. ac.	Nil b.	Yell. pp.	Nil b. & a.	Nil.	Nil.	Nil.	Nil.
16	1.053	70	Misc.	Neut.	Bl. vi. b. buff pp. a.	Wh. pp.	Nil.	Nil.	Bl. pp. comes slow.	Nil.	v. sl. pp.
17	—	100 (ap- prox.).	5	Ac.	Bl. to gr. bl. b., br. bl. pp. a.	Nil.	Br. b. & a.	Nil.	Dirty br. pp.	Nil.	Nil.
18	1.125 for 25°c	Misc.	Misc.	St'g. ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
19	—	v. sl.	30	Mod. ac.	Nil b. & a.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
20	—	1	1½	Ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
21	—	Sl	48	Ac.	Deep red col. b. pp. a.	De- cols. first few dps of test.	Nil b. sl. re- duc- tion a.	Nil.	Nil.	Nil.	Nil.
22	—	Almost insol.	Insol.	Faint ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
23	0.898	Insol.	55	Ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.

No.	SUBSTANCE.	HEAT.	HEAT C. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub> .	N.P.S. & Hal.	M. Pt. (°C)
24	Acid Oxalic ...	M. & sub.	Nil.	Nil.	De-comps. to CO <sub>2</sub> , CO, & H <sub>2</sub> O.	Nil.	Nil.	102°
25	„ Pyrogall-lic	Sub. c. decomp	Br. to greenish yell.	Yell. col.	Ch. quick.	Br. violent eff.	Nil.	132°
26	„ Salicylic	Sub. vap. burns	Nil.	Nil.	Sl. br. not ch.	Nil.	Nil.	156°
27	„ Sclerotic	Ch. alk. vap. burns	Strong Alk. vap.	Nil.	Ch. quick	Nil.	N.	Nil.
28	„ Stearic ...	Sub. vap. burns	Nil.	Yell.	Ch.	Nil.	Nil.	50-55
29	„ Succinic	M & vol.	Vap. burns	Nil.	Ch. & sl. sub.	Nil.	Nil.	182°
30	„ Tannic	Part m. ch orange sub. & br. inflam. vap.	Dirty br.	Dirty br.	Br. then deep vi. and ch.	Br. c. eff.	Nil.	Nil.
31	„ Tartaric	M. ch. vap. burns	Nil.	Nil.	Eff. vap. burns	Nil.	Nil.	162-165
32	„ Valerian-ic	Evap. c. str. odors, vap. burns	Nil.	Darkens sl.	Ch. quick.	Nil.	Nil.	—
33	Acidol <i>vide</i> Betaine H Cl	—	—	—	—	—	—	—
34	Acoine ...	M. yell. liq. ch. alk. vap. burns	Bl floats on soda & gives Isonitrite-like odor	Sl. eff. otherwise nil.	Ch. quick	Br. to bl.	N. & Cl.	173°
35	Aconitina ...	Ch. c acrid vap.	Fruity odor at first.	Nil.	Ch. c Ac. Benzoic odor	Nil.	N.	190 approx.
36	Adrenalin ...	Red sh ch. alk. vap.	Br. froth Bl. alk. vap.	Yell. col.	Ch. quick.	Yell. br. c sl. eff.	N.	—
37	Æsculin ...	M. c. sl eff. ch. yel. dist. vap. burns.	Froths, darkens sl. vap. burns.	Darkens sl.	Red br. ch. quick.	Yell. br. c. sl. eff.	Nil.	—
38	Æthyl Bromid	Evap.	Nil.	Nil.	Nil.	Nil.	Br.	—



[illegible]

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
39	Æthyl Chlorid	Evap.	Nil.	Nil.	Nil.	Nil.	Cl.	—
40	Æthyl Iodid...	Evap.	Nil.	Nil.	Gives off I.	Sl. dark- ening	I.	—
41	Albumin Tan- nas ... ..	Ch. c. odor of burnt feathers Br. alk. vap. burns.	Br. c. odor of burnt feathers alk. vap	V. dark br.	Ch. immedi- ately.	Br. & swells up.	N & S.	—
42	Alcohol Meth- ylic ...	Evap.	Br.	Ch.	Ch.	Br.	Nil.	—
43	Aldehyde Abs.	Evaps.	Ch.	Instant ch. & swells up.	h, im- me- diate.	Dark- ens sl.	Nil.	—
44	Alloxan ...	M. to dark red br. liq. ch. & gives HCN. odor.	Blue in cold & color- less on heating alk. vap.	Nil.	Yell. but does not ch.	Nil.	N.	—
45	Aloes Barb. ...	Part m. br. yell. vap. burns. br. dist.	Red to br. col.	Br.	Ch..	Red.	Nil.	—
46	" Cape ...	Part m. br. yell. vap. burns. br. dist.	Red to br. col.	Br.	Ch.	Dirty br.	Nil.	—
47	" Soc. ...	Part m. br. yell. vap. burns. br. dist.	Red to br. col.	Red br.	Ch.	Red-br.	Nil.	—
48	Aloin ...	M. & Ch. vap. burns.	Ch.	Br.	Ch.	Deep red.	Nil.	145



No.	SP. GR.	SOL. Aq. (1 in—).	SOL. ALC. (1 in—)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. Aq.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
39	0.911 to 0.916 at 8° C., U.S.	Sl.	Read- ily	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
40	1.94	400	Misc.	Sl. ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
41	—	Sl.	Sl.	Sl. acid.	Bl. col. b. Br. pp. a.	Nil.	Nil.	Nil.	Dark dirty br. pp.	Nil.	Nil.
42	0.796 to 0.81.	Misc.	Misc.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
43	0.7876	Misc.	Misc.	Mod. ac.	Nil.	Nil.	Re- duct. b.	Nil.	Nil.	Nil.	Nil.
44	—	Sl.	Sl.	Ac.	Nil.	Nil.	Nil.	Nil.	Sl. blue col.	Nil.	Nil.
45	—	Part. sol.	6 in- com- plete.	Faint ac.	Vi. br.	Yell. pp.	Br. gr.	Nil.	Red col.	Nil.	Br. pp.
46	—	Part. sol.	2	Faint ac.	Vi. br.	Yell. pp.	Br. col.	Nil.	Br. pp (Red to vi. col.— Sch- midt.)	Nil.	Br. pp.
47	—	Part. sol.	8 in- com- plete.	Faint ac.	Vi. br.	Yell. pp.	Br. gr.	Nil.	Nil.	Nil.	Br. pp.
48	—	140	20	Faint ac.	Vi. br. b. & a.	Yell. pp.	Br. col. b. & a.	Nil.	Red col.	Nil.	pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
49	Alphogen ...	First eff. ch. c cryst. sub.	White cryst. sub. & ch.	Nil.	Eff. & ch.	Eff. no col.	Nil.	262° c. de- com
50	Aluminii Aceto-Tart.	Ch. vap. burns	Vap. burns.	Nil.	Ch.	Nil.	Nil.	Nil.
51	Alypin ...	M. c. eff. then ch. Alk. vap. burns	M. & floats on soda.	Eff. str.	Goes br., not ch.	Nil.	N. & Cl.	169
52	Amylene Chloral Sol. 1:1	Evaps. vap. burns.	Nil.	Dark'ns sl.	Separates, vap. burns c. gr. flame	Nil.	Cl.	—
53	Amylene Hydrate	Evaps.	Nil.	Nil.	Ch.	Nil.	Nil.	—
54	Amyl Nitris ...	Evaps. sl. res. ch.	Gr. c Alk. vap.	Blue, rapidly to br.	Ch.	Dark'ns slowly	N.	—
55	Amyl Val- erianas	Evaps. vap. burns.	Ether'l odor, vap. burns	Dark'ns sl.	Dark rd. br., ch. & vap. burns c. garlic odor	Nil.	Nil.	—
56	Anæsthesine...	M. evap. vap. burns.	Froths sl. and vap. burns	Ch. v. slowly	Nil.	Nil.	N.	89
57	Anhydro- Glyco-Choral	M. ch. c. br. dist.	Br. c. caramel odor vap. burns.	Nil.	Ch. quick c. Chloral odor.	Nil.	Cl.	187°
58	Anilin ...	Evaps.	Nil.	Forms br. solid and gets hot	Ch. slowly	Forms pink solid.	N.	—
59	Anthrarobin ...	Br. sub. v. wh. res.	deep purple	Dark br.	Red br. sol. & ch. quick	Eff. nearly br.	Nil.	—
60	Antim. Pot. Tart.	Blackens, grey-wh. sub.	Bl.	Nil.	Ch. quick.	Nil.	(Antim. in bl. residue)	—





No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
61	Antipyrin, see Phenazon	—	—	—	—	—	—	—
62	Aphrodine ...	M. to br. liq. c. beastly odor, ch. alk. vap. burns	M. to br. mass on surface of NaOH	Nil.	Pink-vi. then gr. br.	Gr. yell.	N. & Cl.	—
63	Apiol (Green Liquid)	Goes br. br. dist.	Goes bl. & gives milky dist. pung. & wh. vap.	Br. and viscid.	Ch. c. much eff.	Eff. sl. c. br. col.	Nil.	—
64	Apocodeine HCl.	Smell of burnt feathers	Alk. vap.	Dark- ens sl.	Ch.	Eff. and turns br.	N. & Cl.	Prt. a 90 de- c'm. ov'r 200
65	Apomorphine HCl.	Ch. c. wh. vap.	Dark'ns	Nil.	Ch.	Crim. to yel. in 2 mins.	N. Cl.	—
66	Arbutin ...	M. c. sl. eff. then ch. br. dist. & vap. burns.	Froths a lot, darkens vap. burns	Red col.	Dark red and ch. quickly	Red-br. sl. c. eff.	Nil.	166
67	Argenti Fluorid.	Vap. corrod's glass.	Nil.	Nil.	Wh. vap corrod's glass.	Nil.	F.	Nil.
68	Argenti Lactas	Ch. vap. burns.	El.	Nil.	Ch.	Nil.	Nil.	Nil.
69	Argenti Proteinas	Ch. br. dist. alk. vap. burns	Bl. wells and alk. vap. burns	Nil.	Ch. almost immed. and vap. burns	Nil.	N.	—



No.	Sp. Gr.	SOL. Aq. (1 in -)	SOL ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	Br. Aq.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CH <sub>3</sub> .	ACID PIC- RIC.	DRAG.
61	—	—	—	—	—	—	—	—	—	—	—
62	—	Sl.	130	Neut.	Nil.	Yell. pp. rediss at first	Wh. pp. b. & a.	Wh. pp.	Vi. br. pp.	Yell. pp.	Red br. pp.
63	1.07	Prac. insol.	Part.	Prac. Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Br. pp.
64	—	1	1	Neut.	Drkns b. & a.	Dirty br. pp.	Drkns b. dirty gr. pp. a.	Dirty buff pp.	Dirty br. pp.	Yell. pp.	Br. pp.
65	—	69	51	Neut.	Vi. b. & a.	Red pp.	Nil.	Wh. pp.	Br. rd pp.	Yell. pp.	Br. pp.
66	—	10	13	Neut.	Blue b. br. a	Yell. pp. c. excess br.	Nil.	Nil.	Gr. cl. coming slwly to br. pp.	Nil.	Nil.
67	—	2	3	Fa'nt- ly alk.	Wh. pp.	Wh. pp.	Bl. pp.	Yell. pp.	Light choc. pp.	N'dle cryst. on st'nd- ing.	Br. pp. to wh.
68	—	18	500	Neut.	Wh. pp.	Wh. pp.	Bl. pp.	Yell. pp.	Light br. pp.	Sl. pp.	Br. pp to wh
69	—	Imper- fectly.	V. sl.	Sl. alk.	Sl. opale- scence b., fr'thy a.	Wh. pp.	Nil. b. br. col. a.	Light- ens in col.	Nil.	Yell. floccy pp.	Br. pp. turn- ing wh.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. f t. (°C
70	Argonin	... Ch., br. dist., alk.vap. & nitrogenous odor.	Bl. c. strong alk.vap.	Yell.	Ch.	Nil.	N.	Nil.
71	Argyrol...	... Swells up & Ch.	Alk. vap.	Grey.	Ch.	Wh. & eff.	N. & S.	Nil.
72	Arrhenal	Ch., bl. sub. garlic odor.	Nil.	Nil.	Nil.	Nil.	Nil	Nil.
73	Arsamin	Ch. bl. sub. & alk. vap.	Nil.	Nil.	Ch. v. slowly	Nil.	N.	—
74	Asparagin	... Red br., alk. vap.	Darkens alk. vap. & nitrogenous smell.	Nil.	Ch. slow.	Nil.	N.	—
75	Atropine Methyl Brom.	M. c. sl. eff. ch. & gives. br. dist. & irrit. vap.	Red br. and gives alk.vap.	Eff. and turns sl. yell.	Ch. quick	Nil.	N. & Br.	214
76	Atropine and Salts	Base m. and sub. b. ch. salts m. and ch.	Br. pungent alk. vap. burns.	Nil.	Ch.	Nil.	N (S. in Atropine Sulph.)	B'se 115° Sul. 187°
77	Benzol ...	... Evap. vap. burns.	Nil.	Nil.	Ch. slowly vap. burns.	Nil.	Nil.	Nil.
78	Benzopiperaz <i>vide</i> PIPERAZ. BENZ.	—	—	—	—	—	—	—





No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N. P. S. & Hal.	M. Pt. (°C)
79	Betaine HCl....	Part m., ch. c. eff. and alk. vap. burns.	Alk. vap.	Eff.	Eff. not ch.	Nil.	N. Cl.	—
80	Betol. ...	M. turns yell. part evap. ch. vap. burns.	Yell.	Nil.	Goes from yell. to gr. bl. and ch.	Nil.	Nil.	95
81	Bismuthi Benzoas	Bl. c. yell. sub. and wh. vap. c. Ben- zoic odor.	Bl. c. B'nzene odor, vap. burns.	Nil.	Nil.	Nil.	Nil.	Nil.
82	„ Citras ...	Bl. c. bl. sub.	Bl.	Nil.	Eff. and vap. burns ch. slowly.	Nil.	Nil.	Nil.
83	„ Oxy- Iodogall.	Iodine vapour (bl)	Nil.	Ch.	Strong Iodine (vi.) vap.	Eff. & I. vap. emitted	I.	—
84	„ Salicyl. ...	Black- ens vap. c. odor of Phenol burns.	Bl.	Nil.	Gradu- ally goes br. eff.	Br. in parts only.	Nil.	Nil.
85	„ Subgallas	Goes bl. vap. burns.	Goes bl.	Nil.	Turns red c. wh. pp. then bl.	Dark. gr. & eff finally br.	Nil.	Nil.
86	Bromal- hydrate	M. wh. vap. colors flame green.	Bromo- form odor.	Nil.	M. does not mix, yell. dist.	Sl. yell.	Br.	54
87	Bromethyl Formine	Eff. ch. c. alk. vap.	Wh. alk. vap. c. Pyridin odor burns.	Sl. br.	Yell. vap. col flame gr.	Sl. yell. to br.	Br. N.	200 Sch mdt



No.	SP. GR.	SOL. Aq. (1 in -).	SOL. ALC. (1 in -).	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. Aq.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
79	—	2	About 20	Acid.	Nil.	Pp. rediss at first.	Nil.	Nil.	Nil.	Cryst. pp. in conc. Nil in di- lute.	Br. pp.
80	—	Almost insol.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
81	—	Almost insol.	Al- most insol.	Sl. acid.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
82	—	Almost insol.	Insol.	Faint acid.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
83	—	v. sl. Iodide & Gallic Acid go into solution	In- com- plete- ly sol.	Sl. ac.	Bl.	Nil.	Nil.	Nil.	Yell. pp.	Nil.	Nil.
84	—	Almost insol.	Al- most insol.	Neut.	Vi. col. turns br. a.	Yell. pp.	Nil.	Nil.	Nil.	Nil.	Nil.
85	—	Insol.	Insol.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
86	—	2½	½	Neut.	Nil.	Nil.	V. light bl. pp. b. dis- solves a.	Nil.	Nil.	Nil.	Nil.
87	—	0·6	25	Neut.	Nil.	Yell. pp.	Nil b. sl. reduc. a.	Yell. pp. ch'ng- ing to wh.	Br. yell. pp.	Cryst. pp. comes slowly.	Red br. pp

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	Mt. P. (°C)
88	Brometone ...	M., sub. and ch. c.v. irri- tating vap.	Vap. burns,	Nil.	Forms red drops v. irritat- ing vap.	Nil.	Br.	167
89	Bromoform ...	Dist. then ch. c. br. vap. Brom. odor.	Dark'ns & vap. flame gr.	Nil.	Goes br. with br. vap. & then color- less.	Nil.	Br.	—
90	Bromo- Valerianyl- Urea.	M. ch., orange sub.and vap. burns.	Str.alk vap. burns, darkens sl.	Nil.	Red br. c. valer- ian odor, no ch.	Nil.	N. and Br.	138 to 143
91	Butyl Chloral	Sub. totally.	Dark'ns	Nil.	Ch.	Nil.	Br.	78
92	Caffeine... ..	Sub. & m.	Sl. sub. & alk. vap.	Nil.	Yell. slowly, no ch.	Nil.	N.	236°
93	Caffeine... Citras	M. ch. c. br. dist. & sl. vap. burns c. Phenol odor.	Alk. vap. & eff. a lot.	Deli- cate pink.	Eff. & ch. slow.	Nil.	N.	162°
94	Caffeine So- dio-Salicyl	Part m. sub. c. alk. vap.	Alk. vap. & eff. a lot.	Nil.	Ch. slow.	Nil.	N.	Nil.
95	Calcii di- Bromo- behenas	Part m. ch. c. gr. br. dist. vap. burns	Oily odor and darkens sl.	Sl. br.	Br. and ch. c. much eff.	Oily	Br.	Abt 230
96	Calcii Gly- ceroph.	Ch. acid vap. burns.	Eff. vap. burns. Sl. black- ens.	Nil.	Ch.	Nil.	P.	Nil.
97	Calcii Lactas.	M. swells & ch.	Eff. vap. burns.	Nil.	Eff. ch. vap. burns c. blue flame.	Nil.	Nil.	Nil.





NO.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
96	Calcii Saccharas	Ch. c. caramel odor.	Br. & vap. burns.	Br.	Ch. at once.	Eff. sl.	Nil.	Nil.
97	Camph. Monobrom.	M. c. camph. odor & sub.	Camph. odor vap. burns.	Nil.	Yell. & ch. quick.	Liquefies.	Br.	76
98	Cannabin Tannas	Part. m., wh. alk. vap. & br. dist. c. tobacco odor.	Br. c. br. dist. & alk. vap.	Darkens.	Ch. at once.	Eff. yell.-br.	N. difficult to detect.	Nil.
99	Cantharidin ...	M. sub. vap. burns.	Darkens.	Nil.	Ch. quick.	Nil.	Nil.	218
100	Capsicin ...	Boils, irrit. vap. burns.	Irrit. vap. burns.	Ch. at once.	Ch. at once, c. eff.	Nil.	Nil.	—
101	Carbamide. <i>See UREA.</i>	—	—	—	—	—	—	—
102	Chinolin ...	Evaps. & vap. burns.	Vap. burns.	Gets hot & solid.	Br. slow.	Forms crystals slowly.	N.	—
103	Chinosol ...	M. c. eff.	Bl. c. odor like Chin'lin	Nil.	Br. slow.	Eff. sl. gives br.	N,S.	172
104	Chloralamid ...	M. sub. c. chloral odor.	Eff. alk. vap. c. Isonitrile odor. alk. vap. burns.	Nil.	Eff. c. Chloral odor no ch.	Nil.	N,Cl.	115
105	Chloral Hydras	M. sub. c. distinctive odor.	Eff. a lot.	Nil.	Irrit. vap. not ch.	Nil.	Cl.	48-49



No.	SP. GR.	SOL. Aq. (1 in -).	SOL. ALC. (lin-).	LIT. MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b & a. boil.	BR. AQ.	FREU- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
96	—	10	In- sol.	Alk.	Pp. b., nil a.	Nil.	Nil.	Nil.	Sl. yell. pp.	Nil.	Sl. br. pp.
97	—	Insol.	18	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
98	—	Sl.	Sl.	Sl. ac.	Black b. & a.	Nil.	Bl.- gr. col. b., gelat. pp. a.	Slight buff pp.	Bl. pp.	Nil.	Red- br.
99	—	400	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
100	0.918	V. sl.	Misc.	Sl. ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Red- br.
101	—	—	—	—	—	—	—	—	—	—	—
102	1.09	Sl.	Misc.	Sl. alk.	Nil.	Yell. pp.	Sl. pp. b., nil a.	Wh. pp.	Crm. pp.	Yell. pp.	Red- br. to bl.
103	—	1	Sl.	Sl. ac.	Dark green pp. b. bl., a.	Yell.	Yell. gr. b. & a.	Crm. pp.	Buff pp.	Yell.	Red- br. to bl.
104	—	20	2	Neut.	Nil.	Nil.	Nil b. red a.	Nil.	Nil.	Nil.	Nil.
105	—	0.25	0.2	Neut.	Nil.	Nil.	Blue pp. b., re- duc- tion and smell CHCl <sub>3</sub>	Nil.	Nil.	Nil.	Nil.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
106	Chloretone ...	Wh. sub. & irrit. vap.	Br. vap. burns c. gr. edg.flm.	Nil.	Eff. c. irrit. vap.	Nil.	Cl.	80
107	Chrysarobin (ACID CHRYSOPHANIC)	M. ch. & yell. vap. burns	Black-ens	Yell.	Deep red ch. quick	Nil.	Nil.	152-4
103	Cimicifugin ...	Br. dist. vap. burns	Nil.	Br.	Ch. quick	Br.	N.	Nil.
109	Cinchonidine	M. ch. & alk vap. burns	Orange br. & floats on soda	Nil.	Ch. slow	Nil.	N.	202
110	Cinchonine ...	M. ch. c. burnt feather odor & alk. vp. bus.	Alk. vp. Pyridne odor	Nil.	Ch. slow	Nil.	N.	255
111	Cinnamic Aldehyde	Evap. res. ch. vap. burns	Br. c. aromat. vap. burns	Ch. immedi.	Ch. at once	Goes darker & solid	Nil.	—
112	Citrophen ...	M. c. de-comp. yell. sb. vap. burns	Alk. vap. burns	Nil.	Eff. ch. slowly vap. burns	Blue	N.	170c dec-omp
113	Citric Acid <i>vide</i> ACID	—	—	—	—	—	—	—
114	Cocaine ...	M. c. yell. dist. ch. & alk. vap. burns	Turns buff col. c. alk. vap.	Nil.	Turns br. ch.	Nil.	N.	98
115	Cocaine Hydrochlor	M. c. eff. to yell. liq. ch. & alk. vap. burns	Buff col. c. alk. vap.	Eff.	Turns br. ch.	Nil.	N. & Cl.	182c dec-omp
116	Codeine Hydrochlor	M. to br. liq. c. eff. ch. br. dist. & vap. burns	Br. c. alk. vap.	Eff. darkens sl.	Eff. trns sl. vi. then br. & ch.	Eff. c. yell-br. col.	N. & Cl.	255



No.	SP. GR.	SOL. AQ. (1 in -).	SOL. ALC. (1 in -).	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b & a. boil.	BR. AQ.	FER- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAQ
106	—	200	1½	Neut.	Nil.	Nil.	Nil b. gr. to yell. pp. a.	Nil.	Nil.	Nil.	Nil.
107	—	V.sl.	V.sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
108	—	Sl.	1	Neu.	Nil. b strin- gy pp. a.	V. sl. pp.	Nil. b. sl. red pp. a.	Nil.	Nil.	Nil.	Sl. br. pp.
109	—	V.sl.	20	Prac. neut.	Nil.	Yell. pp.	Nil.	Wh. pp.	Buff pp.	Yell. pp.	Red br. pp.
110	—	V.sl.	175	Prac. neut.	Nil.	Yell. pp.	V. sl. pp. b. floccy wh. pp. a.	Wh. pp.	Buff pp.	Yell. pp.	Red br. pp.
111	1.057	Sl.	Misc.	Prac. neut.	Nil.	Sl. floccy pp.	Nil.	V. sl. pp.	Nil.	Nil.	Red br. pp.
112	—	180	Sl.	Acid	Sl. pp. b. deep red col. & pp.	Yell. pp.	Nil.	Nil.	Vi. pp.	Nil. at first yell. d'l'e'te crysts form slwly	Nil at first grad. goes vi.
113	—	—	—	—	—	—	—	—	—	—	—
114	—	Sl.	10	Alk.	Nil.	Yell. pp.	Nil.	Wh. pp.	Buff pp.	—	Red br. pp.
115	—	0.5	2½	Neut.	Nil. b. sl. br. pp. a.	Yell. pp.	Wh. pp. b. to oily drops a.	Wh. pp.	Yell. pp.	Yell. pp.	Red br. pp.
116	—	30	26	Neut.	Nil.	Yell. pp. redis at first	Nil.	Wh. pp.	Lt. br. pp.	Yell. pp.	Red br. pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N. P. S. & Hal.	M. Pt (°C)
117	Colchicine ...	M. c. d'comp. ch. alk. vap. burns.	Turns deep br. c. alk. vap.	Br.- yell.	Br. to deep red.	Deep vi.	N.	143 de- com. at 147
118	Colchicine Salicyl	M. c. d'comp. ch. alk. vap. burns.	Deep. br. c. alk. vap.	Br. yell.	Br. to deep red.	Deep vi.	N.	55- 60
119	Coninæ HBr...	M. and evaps. c. br. dist.	Alk. vap. burns.	Br. yell.	Red br. no ch. c. br. vap.	Nil.	N. and Br.	214
120	Cotarnin HCl.	Deep red & m. partly ch. & br. alk. vap. burns.	Red c. nause- ous odor, then br. alk. vap. burns.	Eff. & darkens sl.	Deep ma- genta slowly. Does not ch.	Br. orange.	N. & Cl.	Abt 191 Ha- ger (Pt. 125) (see also text 98
121	Cotarnin Phthalas	M. to deep red liq. Ch. br. dist. & alk. vap. burns.	Br. c. nause- ous odor & alk. vap.	Gr. yell.	Ma- genta & does not ch.	Orange.	N.	98
122	Coumarin ...	M. and evap. vap. burns.	Yell. vap. burns.	Nil.	Br. no ch.	Nil.	Nil.	67
123	Credé's Silver	Br. sub. & alk. vap. burns.	Alk. vap. burns.	Nil.	Nil.	Eff. and dirty grey col.	N.	Nil
124	Cresylic Acid <i>vide</i> ACID	—	—	—	—	—	—	—



[illegible]

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
125	Cryogenin ...	M. ch. str. alk. vap. burns.	Alk. vap. burns.	Sl. pink	Deep blue and ch.	Eff. and br. col.	N.	170
126	Cubebin ...	M. ch. c. br. dist. & vap. burns	Yell. mass floats on soda.	Deep red.	Deep red ch. quick.	Br. to gr.	Nil.	128
127	Dextrose (Commercial).	Ch. odor of burnt sugar, br. sub. vap. burns.	Goes br.	Nil.	Ch. immed.	Nil.	Nil.	Nil.
128	Di-Bromo Tannin Gelatin	Ch. c. nitro- genous odor.	Br. c. eff.	Dark'ns sl.	Ch.	Yell. br. c. eff.	Br. N.	Nil.
129	Diacetyl- Morphine	M. then ch. alk. vap. burns.	Deep orange sl. alk. vap.	Sl. br.	Ch. fairly quick	Yell.	N.	169
130	Diacetyl- Morphine HCl.	M. to br. liq. c. sl. eff. alk. vap. burns.	Deep orange froths a lot sl. alk. vap.	Sl. br. c. sl. eff.	Ch. fairly quick	Yell.	N. & Cl.	233
131	Digitoxin ...	M. ch. yell. dist. vap. burns.	Goes dark & floats on soda as a bl. mass.	Ch. to br. mass.	Chars immed.	Yell. to vi.	Nil.	240
132	Dimethyl Piperazine Tartras	Part. m. and ch. & gives br. alk. vap. burns	Alk. vap.	Nil.	Goes br. and ch.	Nil.	N.	250 Hager.
133	Elaterin ...	M. to yell. liq. c. eff. br. dist. vap. burns	Yell. then br. mass on soda	Br.	Deep red br. & ch.	Nil.	Nil.	209
134	Emetina ...	Part. m. & ch. alk. vap. burns	Floats as br. mass on soda	Dirty br.	Br. & ch. slowly	Br.	N.	69



No.	SP. GR.	SOL. Aq. (1 in -).	SOL. ALC. (1 in-)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
125	—	100	25	Neut.	Nil.	Nil.	Gr. col. b. reduc- tion a	Nil.	Bl. br. pp.	Nil.	Br. yell. crysts form sl'wly
126	—	V. sl.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
127	—	Misc.	Sl.	Neut.	Nil.	Nil.	Nil. Str. re- duct. a.	Nil.	Nil.	Nil.	Nil.
128	—	Almost insol.	Part. sol.	Sl. acid.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
129	—	Sl.	44	Sl. Alk.	Nil.	Yell. pp.	Nil.	Sl. wh. pp.	Sl. buff. pp.	Sl. yell. pp.	Red br. pp.
130	—	2½	13	Neut.	Nil.	Yell. pp.	Wh. pp. b. clot- ting. a.	Wh. pp.	Dirty yell. pp.	Yell. pp.	Red br. pp.
131	—	Pract. insol.	140	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
132	—	2	Sl.	Sl. acid.	Nil b. and a.	Yell. pp. redis- solves at first.	Nil b., and a.	Nil.	Blue bl. col. comes slow- ly.	Yell. pp.	Br. bl. pp.
133	—	Insol.	160	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
134	—	Sl.	3	Sl. alk.	Nil.	Sl. dark yell. pp.	Nil.	Very sl. wh. pp.	Very sl. dirty cream pp.	Sl. yell. pp.	Dark red br. pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
135	Enesol (Hyd., ARSEN. SALICYL.	Bl. c. metallic sub. & garlic odor	Bl. & a grey deposit creeps up tube	Nil.	Red br. eff. quickly darkens	Nil.	Nil.	Nil.
136	Ephedrine HCl.	M. & gives arom. odor, ch	Alk. vap.	Eff. sl.	Eff. ch. quick	Nil.	N. & Cl.	211
137	Epicarín ...	M. to br. liq. ch. & vap. burns c. odor of Naph.	Red, quickly to yell.	Br.	Deep br. red & ch. slowly	Eff. & goes red	Nil.	199
138	Ergotinine ...	Bl. c part fusion	Floats as bl. mass on Soda & gives alk. vap.	Gr. br.	Gr. br. & ch. quickly	Br.	N.	Blk at 210
139	Erythrol Nitrate	M. & then ex- plodes	Nil.	Nil.	Br. then wh. again, does n't ch.	Nil.	N. This test must be used c. caution	61
140	Ethyl-Mor- phine HCl.	M.c. eff. & gives fish odor. ch. vap. burns.	M. to br. sub- stance on sur- face of soda.	Eff. sl.	Eff. br. tinge changing to faint blue ch. slowly.	Eff. sl. & goes red. br.	N. & Cl.	124
141	Eucaín Lactate	M. & evaps., a lot, & vap. burns	Froths a lot, & vap. burns	Nil.	Ch. quickly	Nil.	N.	155
142	Eucalyptol ...	Evaps., vap. burns & euca- lyptus odor	Sl. br., & vap. burns	Br.	Red br. & ch. to a resino's solid	Nil.	Nil.	—



No.	S.P. GR.	SOL. Aq. (1 in -).	SOL. ALC. (lin-).	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	Br. Aq.	FEE- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG
135	—	Sl. sol.	Alm. insol.	Mod. ac.	Vi. col. b. & a.	Wh. pp.	Nil b. sl. opal. a.	Nil.	Nil.	Nil.	Sl yell. pp.
136	—	7	8	Neut.	Nil.	Yell. pp. rediss & repp. by exce's	Nil.	Nil.	Nil.	Nil.	Red br. pp
137	—	V. sl.	7	Faint- ly ac.	Vi. cl. b., br. col. a.	V. sl. pp.	Nil.	Nil.	Nil.	Nil.	Nil.
138	—	Insol.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
139	—	Insol.	Abo't 90	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
140	—	10	25	Neut.	Nil. b. sl. br. pp. a.	Yell. pp. rediss at first.	Light blue pp. b. oily drops a.	Wh. pp.	Br. yeli. pp.	Yell. pp.	Br. pp.
141	—	5	8	Faint- ly alk.	Sl. cloud b., sl. br., pp. a.	Wh. pp.	Wh. pp. b. separ- ates as oily drops a.	Wh. pp.	Cr'am pp.	Yell. pp.	Red br. res. pp.
142	0.93	Slightly	Misc.	Neut.	Nil b., sl. opal a.	V. sl. pp. rediss at first	Nil.	Nil.	Nil.	Nil.	Br. pp.

No.	SUBSTANCE.	HEAT.	HEAT. c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub> .	N.P.S. & Hal.	M. Pt. (°C)
143	Euresol ..	..	Bright red nr. edge of liq. Acetic odor, vap. burns & ch.	Yell. but if not thoroughly mixed patches of red	Yell.-gr.	Olive gr. ch. slowly	Br. Nil.	—
144	Eurobin	...	M. & ch. vap. burns	Bl.	Red & turns to br.	Red sol. quick ch.	Br. Nil.	Abt. 94
145	Exalgine	...	M. & sub.	Benzol odor, vap. burns	Nil.	Nil.	Nil. N.	101
146	Fluorescein	...	Part m. turns br. gr. ch. & swells up	Vi. to bl. then yell.	Nil.	Yell. dissolves, turns red-br.	Turns yell. immediately	Nil. —
147	Formalin	...	Boils, gives gas burns blue, sl. res. ch.	Goes br. quick before heating. Vap. burns	Forms glassy looking solid.	Ch. quick	Eff. after a time, goes. gr. at edges	Nil. —
148	Fuchsin...	...	Part m. & br. vap. burns	Separates fused on surf. of NaOH	Red br.	Ch. quick	Dark br. N. & Cl.	—
149	Gelseminine		M. ch. br. dist. and alk. vap. burns	Floats on Na OH as br. mass	Dkns. sl.	Red & ch. slowly	Gr. col. N.	158 160 Merck
150	Glycosal	...	Sub.	Nil.	Nil	Ch.	V. faint red-vi.	Nil. 63
151	Glycogen	...	Ch. br.-yell. vap. burns	Br. c. alk. vap. burns.	Nil.	Ch. immed.	Nil. N. & S (Impurities only)	—



No.	SP. GR.	SOL. AQ. (1 in --).	SOL. ALC. (1 in --)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
143	1·200	Sl.	Misc.	Neut.	Br. vi. b. br. a.	Yell. pp rediss at first	Nil b. gr. & then br. pp. a.	Nil.	Blu- i h. strks. come very sl'wly	Nil.	Red br. pp.
144	—	Pract. insol.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
145	—	60	Free- ly.	Alk.	Nil.	Wh. pp.	M. & floats on top	Nil.	Nil.	Nil.	Br. pp.
146	—	Less than 1.	2	Turns blue Litm. paper gr.-yl.	Br. pp. b. Br. pp. a.	Or- ange. red pp.	Br. col. b. and a.	Nil.	Bl- br. pp.	Yell. pp. rediss	Bl. pp. goes br.
147	1·08	Misc.	Misc.	Sl. ac.	Nil.	Nil.	Nil b. dark red pp. a.	Nil.	Nil.	Nil.	Nil.
148	—	Slight.	Abt. 20	Neut.	Nil.	Al- most bl. pp. floats, liq. decol.	V. dark pp. b. and a.	Dark pp. sol. turns vi. pink	Dark pp. sol. turns pur- ple	Br. pp. sol. yell.	Dark pp. sol. gr.
149	—	Sl.	Sol.	Alk.	Nil.	Yell. pp.	Nil b. dirty gr. col. & sl. re- duct a.	Wh. pp.	Light br. pp.	Yell. pp.	Br. pp.
150	—	Sl.	3	Neut.	Deep vi.	Wh. pp.	Nil.	Nil.	Nil.	Nil.	Nil.
151	—	About 2 in- complete	Al- most insol	Faint alk.	Nil b. Sl. pp. a	Sl. wh. pp.	Nil.	Nil.	Nil.	Yell. pp.	Sl. red br. pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
152	Guaiacol ...	Evap. c. char- act. odor vap. burns	Br.	Sl. br.- yell.	Br. & ch.	Dk. br. c. violent re- action	Nil.	—
153	Guaiacol Benzoas	M. and evap., vap. burns.	Sl. br. c. vap. burns.	Yell.	Dark gr. and ch.	Nil.	Nil.	50 to 52
154	Guaiacol Carbonas	M. & evaps. almost entirely vap. burns.	Br. up. tube & vap. burns.	Nil.	Light gr. turns darker & ch.	Nil.	Nil.	86
155	Guaiacol Cinnamas	M. to clear liq. goes br. c. yell. sub. & vap. burns.	Yell. & gives peculiar odor. Vap, burns.	Orange col.	Orange to gr.- br. and ch.	Nil.	Nil.	130 Ha- ger)
156	Hexamethy- len-tetramine	Sub. en- tirely S. m. or ch.	Wh. sub. and sl. alk. vap.	Nil.	Ch. vap. burns	Nil.	N.	—
157	Holocain HCl	M. yell. ch., yel. dist. vap. bns gr. fine	M. br. liq. floats	Sl. eff,	Diss' lvs. c. sl. eff. ch. quick	Nil.	N. Cl.	186— 189
158	Homatropine	M. color less, then ch. br. dist. alk. vap. burns	Eff. a lot, alk. vap. burns	Nil.	Ch. quick	Nil.	N.	98
159	Hydrastine	M. ch. alk. vap. burns	Br. yell. & floats	Nil.	Deep plum col. ch.	Br.	N.	132
160	Hydrastinine HCl	M. to yell. liq. ch. br. dist. vap. burns	Br. c. eff. alk. vap.	Eff. Yell.	Eff. yell. to deep red	—	N. Cl.	6- 117



No.	Sp. Gr.	SOL. Aq. (1 in -).	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. Aq.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
152	1.116	Sl.	Misc.	Neut.	Dk. br. b. Bl. pp. a.	Dk. orange pp.	Nil. b. sl. red pp. a.	Nil.	Bl. pp.	Nil.	Br. pp.
153	—	Almost insol.	50	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
154	—	Nil.	Abt. 200	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
155	—	Insol.	Sol.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil
156	—	1	8	Alk.	Br. pp. b. Red br. a.	Yell. pp.	Nil.	Nil.	Dirty yell.	Cryst. pp. after few secs.	Br. pp. t'ning bl.
157	—	55	8	Faint alk.	Nil.	Yell. pp.	Wh. pp. b. a. clot- ting	Wh. pp.	Buff pp.	Yell. pp.	Br. pp.
158	—	V. sl.	Abt. 3	Alk.	Nil.	Yell. pp.	Nil.	Wb. pp.	Buff pp.	Nil.	Br.
159	—	V. sl.	150	Neut.	Nil.	Sl. cloud.	Nil.	Sl. cloud.	Nil.	Nil.	Sl. br. pp.
160	—	Less than 1	Abt. 5	Neut.	Nil.	Yell. pp.	Nil b. rd. pp. & gr. col. a.	Cr'am wh. pp.	Buff. pp.	Yell. pp.	Red br. pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C.)
161	<b>Hyd. Succinas</b>	Ch. and gives grey sub.	Bl.	Nil.	Sms. to ch. gets light c.wh.pp.	Dark'ns sl.	Nil.	—
162	<b>Hyd. Succini- midum</b>	Ch.grey sub.vap. burns sl. cyanide odor	Bl. c. strong alk. vap.	Nil.	Ch. fairly quick	Dark'ns sl.	N.	Nil.
163	<b>Hyd. Thymol- Acetas</b>	Ch. c. Acetic, then Thymol odor vap. burns.	Yell. then bl., Thymol odor.	Nil.	Yell. then purple & ch.	Deep red br. after little time.	Nil.	Nil.
164	<b>Hyoscine</b> HBr.	M.ch. br.dist. & alk. vap. burns.	Br. & floats on soda.	Eff. & sl. br.	Ch. quick.	Nil.	N., Br.	—
165	<b>Hyoscyamine</b> Sulph.	M. ch. & alk. vap. burns.	Br. floats on soda. Alk.vap	Nil.	Ch. quick.	Nil.	N. & S.	206
166	<b>Hypnal.</b>	M. c. Choral odor ch. & give alk. & inflam. vap.	Bl. & strong Isoni- trile odor.	Nil.	Eff. turns from yell. to br. not ch.	Nil or slight Yell.	N & Cl.	67 68
167	<b>Indigo ...</b>	Odor of HCN. Alk. vap. burns.	Br. c. alk. vap.	Nil.	Color- less & gives wh. pp.	Nil.	N.	—
168	<b>Indigo-Car- mine</b>	Gives off water, nothing else charac- teristic.	Dark brown.	Dis- solves to in- tense bl. sol.	Eff. sl. & dis- solves to blue sol. & ch.	Eff. sl. dis- solves to yell. br. sol.	S. N.	—
169	<b>Iodoform</b>	...	Smell	sufficiently	characteristic.			



No.	SP. GR.	SOL. Aq. (1 in -).	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. Aq.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
161	—	V. sl.	V. sl.	Neut.	Nil.	Nil.	Nil.	Yell. pp. turns red	Nil.	Nil.	Yell. pp.
162	--	28	V. sl.	Alk.	Nil.	Nil.	Sl. opal- esnce. b. wh. pp. a.	Yell. pp. turns orange	Nil.	Nil.	Br. pp. turn- ing cream
163	—	Insol.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
164	—	3	14	Neut.	Nil.	Yell. pp.	Nil.	Wh. pp.	Br. yell. pp.	Yell. pp.	Red br. pp.
165	—	0.5	4	Neut.	Nil.	Yell. pp.	Nil.	Wh. pp.	Yell. pp.	Yell. pp.	Red br. pp.
166	—	10	Abt. $\frac{1}{2}$	Neut.	Deep red col. b. & a.	Yell. pp. re- diss. at first.	Nil b. reduc- ed a.	Sl. wh. cloud.	Buff pp.	Yel. pp.	Br.
167	—	V. sl.	Insol.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
168	—	Sl.	Insol.	Neut.	Deep blue pp. b., br. a.	Dark gr. pp. dis- solv- ing to br. sol.	Gr. col. b., blue col. & sl. red pp. a.	Deep blue pp.	Col. dis- char- ged sl'wly	Nil.	Dark gr. pp.
169	—	—	—	—	—	—	—	—	—	—	—

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
170	Iohydrin	... Br. c. oily dist. vi. vap. burns, & pung- gent res. ch.	Vap. burns, pung- gent odor & goes br.	Dark- ens sl.	Bl.gives vi. vap. & bl. metal- lic sub.	Nil.	I.	—
171	Lactophenin...	M. then ch. and wh. alk. vap. burns.	M. to yell.liq. on sur- face & vap. burns.	Nil.	Ch. slowly vap. burns.	Turns yell. br.	N.	116
172	Lævulose	... M. to br. liq. c. cara- mel odor and ch. vap. burns	Deep br. liq. vap. burns then nearly wh.	Goes br. slowly.	Ch. almost immedi- ately.	Nil.	Nil.	—
173	Lecithin	... M. c. charac- teristic odor.	Wh. alk. vap.	Chars slowly.	Car- bonises.	Nil.	N (small q'antity P.)	—
174	Magnes Ricinoleas <i>Syn. MARICOL</i>	Ch. and pungent vap. burns	Sl. arom. oily odour	Sl. eff.	Eff. ch. quickly	Sl. eff.	Nil.	—
175	Malachite Green	Part m. goes gr. up tube & then br. vap. burns	Goes br. and then wh.	Turns red- dish	Eff. sl. and ch. quick	Turns red colour	N. & Cl.	—
176	Malourea	... M. & sub. en- tirely vap. burns.	Alk. vap. & pecu- liar odor.	Nil.	Ch. slowly.	Nil.	N.	191



No.	SP. GR.	SOL. Aq (1 in -).	SOL. ALC. (1 in -).	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. Aq.	FER- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
170	—	Sl.	Misc.	Neut.	Nil.	Sl. yell. pp. re- dis- solves at first.	Nil.	Sl. wh pp.	Sl. yell. pp.	Nil.	br. pp.
171	—	330	15	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
172	—	Less than 0.5	About 16	Neut.	Nil.	Nil.	Nil b., red pp. a.	Nil.	Nil.	Nil.	Nil.
173	—	Sl.	30 misc. c. 1 but thrws out c. more.	Sl. acid.	Nil.	Dil'te emul- sion gives or- ange pp.	Br. pp.	Nil.	Nil.	Nil.	Or- ange br. pp.
174	—	Almost insol.	V. sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
175	—	2	Abt. 30	Inde- finite	Gr. col. b. Gr. br. a	Dark gr. pp.	Nil b, choc. pp. a.	Dark gr. pp.	Dark gr. pp.	Dark gr. pp.	Dark dirty br. pp.
176	—	150	9	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
177	Mannitol Nitrate	M. goes br. and expldes	Br.gives minute flashes of light then goes al- most wh.	Nil.	Yell. does not ch.	Nil.	N.c. difficul- ty	113
178	Methyl- Amino- Oxybenzoas	M. to Yell. liq. ch. br. dist. & alk. vap. burns.	Goes vi, then gr. c. sl. alk. vap.	Nil.	Br. & ch. slowly.	Blue bl. chang- ing to red-br.	N.	141
179	Methyl- Atropin Nitras	M. eff. ch. & br. dist., & alk.vap. burns	Br., & gives inflam. alk.vap.	Nil.	Br., & turns purplsh	Nil.	N.	149- 150
180	Methyl- Benzoyl Salicyl	Sub. and ch.	Ch.	Nil.	Ch.	Nil.	Nil.	75
181	Methyl- Di Tannin	Ch. c. br. dist. & odor of Tannin. Vap. burns.	Br. then orange then red-br.	Nil.	Int'nslly blue, then ch.	Br. c. sl. eff.	Nil.	—
182	Methylene Blue	Swells and ch. c. sulphur odor	M. and floatson surf. of soda & colors top of tube vi.	Sl. eff. and dark gr.	Eff. a lot and ch. quick	V. dark green	N.S. & Cl.	—
183	Migralgin	M. then ch. and gives br. alk. vap. burns	M. on surf. of soda tns red br. Magenta up sides of tube alk.vap.	Nil.	Yell. does not ch.	Nil.	N.	101- 105
184	Morphine HCl	Ch. c. br. dist.	Orange br. c alk. vap. burns	Sl. eff.	Ch. quick	Red c. sl. eff. & changes to yell.	N. & Cl.	—



No.	Sp. Gr.	Sol. Aq (1 in -).	Sol. Alc. (1 in -).	LIT- MUS.	Fe <sub>2</sub> Cl <sub>3</sub> b. & a. boil.	BR. Aq.	FEH- LINGS b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG
177	—	Almost insol.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
178	—	V. sl.	7	Neut.	Vi. br. col. b., gr. br. pp. a.	Dirty gr. br. pp.	Nil. b., br. red pp. a.	Nil.	Dark gr. pp.	Nil.	V. sl. red br. pp. slow ly.
179	—	1	4	Neut.	Nil.	Wh. pp.	Nil.	Wh. pp.	Cr'am pp.	Nil.	Dull red pp
180	—	Insol.	35	Neut	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
181	—	Sl.	About 3	Neut.	Bl. col. b. br. pp. a.	Nil.	Nil.	Nil.	Vi. col.	Nil.	Nil.
182	—	About 6	Sl.	In- d'finte	Vi. blue b., navy blue a.	Bl. pp. and sol. almost color- less	Nil b. bl. pp. a.	Co- pious blue pp.	Bl. pp.	Red. bl. pp.	Co- pious bl. pp.
183	—	0.3	1	Prac. neut.	Deep red br. b., and a	Yell. pp. re-dis- solving	Nil.	Wh. pp.	Dull. yell. pp.	Bright yell. pp.	Orange red pp.
184	—	24	About 55	Neut.	Blue b. br. yell. a.	Yell. pp. rediss at first	Nil.	Yell. wh. Gelatinous pp.	Yell. br. pp. turns dark'r	Yell. pp.	Red br. pp

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub> .	N.P.S. & Hal.	M. Pt. (°C)
185	Naphthol Bismuth	Goes bl. c. red-br. sub. and vap. burns.	Goes bl.	Dark br.	Goes inky bl. c. wh. pp.	Goes bl.	Nil.	Nil.
186	Nicotine ...	Evaps. c. naus. odor	Charac- teristic choking Nicot. odor	Light red	Red then carbon- ises	Nil at first but pinkish later	N.	—
187	Nitrobenzene	Dist. ch. sl. vap. burns c. smoky flame	Goes br. vap. burns	Nil.	Ch. slowly	Nil.	N.	—
188	Novocain ...	M. to clear liq. ch. c. alk. vap. and naus. odor	Br. to gr. yell. and gives alk. vap.	Eff.	Eff. and goes sl. yell. does not ch.	Nil.	N.Cl.	150
189	Nuclein... ..	Ch. br. alk. vap. burns	Red-br. eff. a lot alk. vap	Almost bl. gummy mass	Ch. at once	Br. gummy mass.	N. & P.	Nil.
190	Orexin TANNAS	Ch. part m. & gives br. dist. sl. alk. vap. burns.	Goes yell.	Goes a dirty gr. br.	Deep vi & then ch. quick	Turns red br. & eff. sl.	N.	Nil.
191	Paraform ...	Part m. and sub. vap. burns	Br. and vap. burns	Nil.	Ch. slowly vap. burns	Eff. violent- ly after a while	Nil.	171
192	Paraldehyde...	Evaps. vap. burns	Vap. burns	Nil.	Ch. almost immed.	Nil.	Nil.	10- 12
193	Pelletierine (SOLID)	M. ch. and alk. vap. burns.	Floats as br. liq. on surface, vap. burns	Nil.	Goes br and ch. slowly	Nil.	N.	46



No.	SP. GR.	SOL. AQ. (1 in-).	SOL. ALC. (1 in-).	LIT- MUS	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BB. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
185	—	V. sl.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
186	—	Misc.	Misc.	Alk.	Br. pp. b. darker pp. a.	Yell. pp. rediss at first	Nil.	Wh. pp.	Buff pp.	Yell, pp.	Br. pp.
187	1:204	Sl.	1	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Light br. pp.
188	—	Less than 1	10	Neut.	Nil.	Yell. pp. rediss finally wh. pp.	Pale blue pp. b., oily drops a.	Wh. pp.	Br. pp.	Yell. pp.	Red- br. pp
189	—	V. sl.	Insol.	Sl. ac.	Nil. b. froth- iness a.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
190	—	Sl.	55	Neut.	Dark gr. tinge b., sl. br. pp. a.	Yell. pp.	Blu- ish op'les cence b. Nil. a.	Wh. pp	Dark buff pp.	Yell. pp.	Red br. pp.
191	—	V. sl.	Sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
192	0.988	10	Misc	Sl. acid	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
193	—	4	3	Alk.	Br. pp. b. and a.	Wh. pp.	Nil.	Nil.	Nil.	Yell. pp.	V. dark br. pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
194	Petrol Ether	Evaps. vap. burns.	Vap. burns	Nil.	Ch. slow vap. burns.	Nil.	Nil.	—
195	Phenacetin ...	M. and volatil- ises almost com- pletely vap. burns	Br. vap, burns	Nil.	Ch. fairly quick	Red br. col.	N.	135
196	Phenalgine ...	Part m. and eff. dense sub. ch. alk.vap. burns	Strong alk. vap. burns	Eff. strong	Goes dark no ch.	Eff. strong	N.	—
197	Phenazone ...	M. then ch. and br. alk. vap. burns	Red br. & goes red vi. up tube and alk.vap. burns	Nil.	Yell. no ch.	Nil.	N.	113
198	Phenazoni Aceto- Salicylas	M. Ace- tic then Phenol- ic inflam. vap.	Red col. creeps up tube.	Nil.	Ch. v. slowly	Br. v. slowly	N.	Abt 45°
199	Phenazoni Salicylas	M. to clear liq. ch. br. dist. and sl. alk.vap. burns.	Magn'ta sub. then br. alk.vap. & ch.	Darkens v. sl.	Br. and chars sl.	Darkens v. sl.	N.	90
200	Phenocoll HCl.	Part m. and ch. br. sub. alk.vap. burns	M. to br. liq. on soda	Eff. sl.	First br. then color- less and ch.	Bright yell.	N. Cl.	—
201	„ Salicyl	M. to br. liq. ch. alk. vap. burns	M. to br. liq. on soda	Nil.	First br. then colorless then br. and ch.	Red. br. eff.	N.	160- 165°C decomps



No.	SP. GR.	SOL. AQ. (1 in -).	SOL. ALC. (1 in -).	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
194	0.670 to 0.700	Insol.	4	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
195	—	Sl.	20	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
196	—	Part	Part	Alk.	Br. pp. b. dark- ening a.	Wh. pp. and eff.	Nil.	Nil.	Sl. dark pp.	Nil	Nil.
197	—	1½	1	Neut.	Deep red b. and a.	Yell. pp. re- diss.	Nil.	Nil.	Buff. pp.	Yell. pp.	Red br. pp.
198	—	160	3½	Ac.	Deep vi. b. & a.	Wh. pp.	Nil.	Wh. pp.	Yell. pp.	Nil.	Red pp.
199	—	200	4½	Acid	Vi. col. b. and a.	Wh. pp.	Nil.	Wh. pp.	Sl. buff. pp.	V. sl. yell. pp.	Red br. pp.
200	—	18	34	Neut.	Nil.	Yell. pp. re- diss. first.	Vi. col. b. vi. br. pp. a.	Wh. pp.	Nil.	Yell. pp. turns cryst.	Br. red pp.
201	—	Sl.	50	Neut.	Vi. col. b., & a.	Wh. pp.	Nil b. sl. vi. br. pp. a.	Nil.	Nil.	Yell. crysts form slwly.	Br. red pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N. P. S. & Hal.	M. Pt. (°C)
202	Phenolph- thalein	M. to br. liq. ch. odor of Phenol. vap. burns	Bl. then deep purple change to dirty orange	Deep red	Red to br. ch. slowly	Yell.	Nil.	250
203	Phloridzin ...	M. c. sl. eff. ch. and gives br dist. and vap. burns	Yell. then br. finally grey c. much eff.	Yell.	Red br. and ch. quick	Bl. to red-br.	Nil.	107 re- sld- fies & m agr. at 170
204	Physostig- mine	M. gives v. irritat- ing vap ch. alk. vap. burns	Br. & alk. vap.	Sl. yell.	Br. yell. changes to gr. & ch.	Yell.	N.	75
205	Physostig- mine Sulph.	M. gives irritat- ing inflam. & alk. vap.	Br. & gives alk. vap.	Sl. yell.	Br. yell. turns gr. & chars.	Yell.	N. S.	140
206	Phytin ...	Ch. br. dist.	Orange red, then gr. Vap. burns	Nil.	Orange pink then br. & ch.	Nil.	P.	Nil.
207	Picrotoxin ...	M. ch. br. dist. vap. burns	Orange yell. to br. c. inflam. gas	Orange yell.	Orange yell. to deep red br. & ch.	Nil.	Nil.	192
208	Pilocarpine ...	Boils, ch. & alk. Vap. burns.	Floats as oily liq. on soda.	Nil.	Ch. slowly.	Nil.	N.	—
209	Pilocarpine Nitrate	Ch. sud- denly alk. Vap. burns.	Floats as oily liq. on soda.	Nil.	Ch. slowly.	Nil.	N.	—



No.	SP. GR.	SOL. AQ. (1 in-).	SOL. ALC. (1 in-)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
202	—	V. sl.	10	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
203	—	V. sl.	4½	Neut.	Vi. br. b., br. col. a.	Sl. yell. pp.	Nil.	Nil.	Nil.	Nil.	Nil.
204	—	Sl.	2	Alk. $\frac{1}{2}$	Nil.	Yell. pp.	Nil. b., br. col. & red pp. a.	Wh. pp.	Br. pp. and pur- plish sol.	Yell. pp.	Red pp.
205	—	Less than 1.	Less than 2.	Faint alk.	Br. col. b., decol- orises & light br. pp. a.	Yell. pp. rediss at first.	Nil. b., br. col. & red pp. a.	Wh. pp.	Fawn pp. turn- ing to bl. c. pur- ple sol.	Yell pp.	Red br. pp. turn- ing orange
206	—	Less than 1 but throws out on dilat- ing.	Insol.	Acid.	Wh. pp. b., & a.	Nil.	Gela- tinous pp. b., almst. rediss Th'wn out agn a.	Nil.	Nil.	Nil.	Sl. Yell pp.
207	—	Sl.	13	Neut.	Nil.	Nil.	Nil. b. sl. pp. a.	Nil.	Nil.	Nil.	Nil.
208	—	V. easily.	Misc.	Alk.	Sl. cloud b., nil. a.	Pale yell. pp. rediss at first.	Nil.	Wh. pp.	Crmy yell. pp.	Sl. yell. pp.	Br red pp
209	—	9	50	Neut	Nil.	Yell. pp. re- diss. at first.	Nil.	Wh. pp.	Crmy yell. pp.	Yell. pp.	Br. red pp.

NO.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
210	Piperazin ...	M. & evaps. completely & alk. vap. burns.	Cryst sub & alk. vap. burns.	Com- bines c. hiss- ing noise.	Nil.	Nil.	N.	104 107
211	Piperazin Benz.	M. & evaps. vap. burns.	Sl. alk. vap.	Nil.	Dark- ens sl. does not ch.	Nil.	N.	Sft- ens 105 M. abt. 167
212	Piperidine Tart.	M. ch. wh. then yell. vap. c. celery odor.	Alk. vap.	Nil.	Ch.	Nil.	N.	Abt 80
213	Podophyllin <i>vide</i> PODOPHYL- LOTOXIN	—	—	—	—	—	—	—
214	Podophyllo- toxin	Part m. ch. br. dist. and vap. burns	Yell. br.	Br. mass gr-yell. on edges	Br. yell. to deep br. and ch.	Eff. and goes choc. br.	Nil.	—
215	Pyramidon ...	M. ch. & alk. vap. burns c. isonit- rile odor.	Goes br. and gives strong isonit. odor.	Nil.	Light r. not char.	Eff. and goes br.	N.	—
216	Quinine ...	M. ch. c. br. dist. & alk. vap. burns.	Orange to gr. yell., & floats as br. mass	Nil.	Yell. & ch. slowly.	Strong fluores- cence.	N.	172
217	Quinine Sulphate	M. to red liq. ch. c. vi. vap. then br. alk. vap. burns.	Orange to gr. yell., floats as br. mass	Nil.	Yell. & ch. slowly.	Strong fluores- cence,	N.S.	205 wh. dr'd ov'r H <sub>2</sub> SO <sub>4</sub>



No.	SP. GR.	SOL. AQ. (1 in -).	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
210	—	2	3	Alk.	Red br. pp. b., & a.	Yell. pp. re- diss. at first.	Nil.	Sl. wh. pp.	Red br. pp.	Sl. yell. pp.	Bl. pp. turn- ing yell.
211	—	100	10	Acid.	Buff pp. b. & a	Yell. pp. re- diss. at first.	Nil.	Nil.	V. sl. buff. pp.	Yell. pp.	Red br. pp.
212	—	Less than 1.	About 30	Acid.	Nil.	Yell. pp.	Nil. b. re- duct- ion slow- ly a.	Wh. crysts form slow- ly	Nil.	Nil.	Br. pp.
213	—	—	—	—	—	—	—	—	—	—	—
214	—	V. sl.	Misc.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
215	—	20	2	Alk.	Vicol. disap- pear- ing b., br. pp. a.	Vicol.	Nil.	Wh. pp.	Vi. col.	Yell. pp. rediss.	Br. pp.
216	—	V. sl.	1	Sl. alk.	Nil.	Yell. pp.	Wh. pp. b. Nil a.	Wh. pp.	Cre'm pp.	Yell. pp.	Br. red pp.
217	—	800	100	Neut.	Nil b. br. pp. a.	Yell. pp. rediss at first.	Wh. pp. b. Nil a.	Wh. pp.	Cre'm pp.	Yell. pp.	Br. red pp.

No.	SUBSTANCE.	HEAT	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
218	Resorcin ..	M. & sub. vap. burns, c. sweet odor.	Red br. and changes to dirty white.	Yell. gr.	Gr. & ch. quick c. much spirt'ng	Yell. to br. slowly.	Nil.	110 C
219	Saccharin ..	M. to clear liq. ch. wh. cryst. sub. & vap. burns c. arom. odor.	Alk. vap. eff. consid.	Nil.	Darkens sl. no ch.	Nil.	N.S.	220
220	Salacetol ...	M. and ch. vap. burns.	Orange col. then fades into muddy col.	Pinkish after a while.	Red. vi and chars. quick.	Nil.	Nil.	67
221	Salicin ...	M. then ch. c. caramel odor.	Br. caramel odor vap. burns.	Red col.	Ch.	Nil.	Nil.	198- 201
222	Salicyl- Salicylas	M. & gives wh. sub. ch. & gives Phenol odor & vap. burns.	Floats as insol. powder on surface of soda.	Nil.	Goes br. does not ch.	Nil.	Nil.	142
223	Sal Limonis ...	Ch. and sl. vap. burns.	Greyish and froths a lot.	Nil.	Ch. quick. vap. burns	Nil.	Nil.	—
224	Salocoll vide PHENOCOLL SALICYL	—	—	—	—	—	—	—
225	Salol ...	M. boils then ch. vap. burns c. Phenol odor.	Turns yell.	Yell.	Ch. slowly	Nil.	Nil.	43



[illegible]

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt (°C)
226	<b>Saloquinine</b> ...	M. ch. alk.vap burns.	Yell. then br.	Nil.	Ch. fairly quick.	Nil.	N.	139
227	<b>Santalol</b> ...	Evaps. vap. burns c. charac- teristic odor.	Yell. br. vap. burns.	Deep red. br.	Deep red br. and chars. quick	Sl. br.	Nil	—
228	<b>Santalol</b> <b>Salicylas</b>	Part evaps.c. charac- teristic odor, vap. burns, res. ch.	Yell.br. and vap. burns.	Red br.	Red br. ch. quick.	Sl. dark	Nil.	—
229	<b>Santonin</b> ...	M. to clear liq. ch. gives br. dist. & vap burns.	Red then br. vap. burns.	Nil.	Yell. to br. and ch.	Nil.	Nil.	170
230	<b>Sodium</b> <b>Anhydro-</b> <b>Methylene-</b> <b>Citrate</b>	Ch.	Nil.	Nil.	Ch.	Nil.	Nil.	Sft- ens at 82 & ch at 250
231	<b>Sodii Cacodyl</b>	Part m. bl. metallic sub., inflam. gas, c. garlic odor.	Eff. a lot	Nil.	Nil.	Nil.	Nil.	—
232	„ <b>Glyceroph</b>	Ch. and irrit. vap. burns.	Dark- ens sl. inflam. gas.	Eff. sl.	Ch. quick	Eff. sl.	P.	—
233	„ <b>p-amino-</b> <b>phenyl</b> <b>Arsonas</b> (see 73)	—	—	—	—	—	—	—
234	<b>Sodii Salicyl</b> ...	Ch. c. odor of Phenol.	Nil.	Nil.	Goes dark, does not ch.	Nil.	Nil.	—



No.	SP. GR.	SOL. Aq. (1 in -)	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. Aq.	FEH- LING'S b. & a. boil.	MAY- ER'S	GOLD CHL.	ACID PIC- RIC.	DRAG.
226	—	V. sl.	120	Neut.	Nil.	Nil.	Nil.	Sl. opal- esce.	Nil.	Nil.	Sl. br. pp.
227	—	Pract. insol.	Misc.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
228	1·012	Pract. insol.	Abt. 40.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
229	—	Sl.	40	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
230	—	1	Sl.	Faint Acid	Br. pp. b.	Yell. pp.	Nil.	Nil.	Yell. pp.	Nil.	Br. pp.
231	—	0·5	1	Alk.	Nil.	Nil.	Nil.	Nil.	Sl. buff pp.	Nil.	Red br. pp.
232	—	0·33 slowly.	Sl.	Alk.	Dark buff pp. b. & a.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
233	—	—	—	—	—	—	—	—	—	—	—
234	—	0·83	5½	Sl. ac.	Vi. col b., vi. pp. a.	Wh. pp.	Nil.	Nil.	Nil.	Nil.	Nil.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
235	<b>Sodii Sulphocarb</b>	Decrep- itates, ch. vap. burns c. Phenol odor.	Nil.	Nil.	Ch. slowly	Nil. at first, turns red slowly	S.	—
236	„ <b>Sulphori- cinas</b>	Evaps. ch. & vap. burns	Eff. a lot and soapy odor	Br. col.	Deep red and ch.	Vi. br.	S. (Cl. impur- ity)	—
237	„ <b>Taurocho- las</b>	Part m., swells up and alk. vap. burns.	Br. & gives alk. vap.	Nil.	Red c. green fluores- cence, and ch. quick.	Nil.	N.S.	—
238	<b>Sparteïn Sulph.</b>	M. boils ch. Pyr- idinic odor. alk. vap. burns.	Alk. vap. & mousy odor.	Nil.	Nil.	Nil.	N.S.	Fir st abt. 62 & ag. 140
239	<b>Stovaine</b> ...	M. vola- tilises ch. c. odor of varnish	Wh. fumes amylic odor.	Eff. no color.	Diss. & ch. on boiling.	Nil.	N. & Cl.	168
240	<b>Strophanthin</b>	Swells ch. c. br. dist. vap. burns.	Pinkish then br. vap. burns.	Em. gr. chang- ing to br. (U.S )	Ch. al- most at once.	Br.	Nil.	Be- gins to fuse at 170 m. at 190 com- plt- ly.
241	<b>Strychnine</b> ...	M. to br. liq. & alk. vap. burns.	Bright red & floats on surface.	Nil.	Ch. slowly.	Nil.	N.	268



No.	SP. GR.	SOL. AQ. (1 in -).	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC	DRA G.
235	—	5	150	Neut.	Vi.col b., br.col & pp. a.	De- color- ised.	Nil.	Nil.	Nil.	Nil.	Nil.
236	—	Misc.	Misc.	Alk.	Buff pp.br. turns br. & m. a.	Yell. pp.	Nil. b. froths a.	Nil.	Nil.	Nil.	Yell. br. pp.
237	—	0.5	About 2	Alk.	Mud. gela- tinous pp. b., br. a.	Res- inous grey- ish pp.	Gr. col. b. red pp. slow- ly a.	Nil.	Nil.	Nil.	Br. resin- ous pp.
238	—	Less than 0.5	6	Ac.	Nil b. Lt.br. pp. a.	Yell. pp. redis. at first.	Wh. pp.b., red- oily drops a.	Wh. pp.	Buff pp.	Yell. pp.	Red br. pp.
239	—	13	3	Pract neut.	Nil.	Yell. pp.	Re- duces on boil- ing.	Wh. pp.	Yell. pr	Yell. pp.	Buff pp.
240	—	Less than 1.	Abt. 1:1	Neut.	Nil.b. lt. br. pp. a.	Nil.	Nil.b. red br. pp. a.	Nil.	Nil.	Nil.	Nil.
241	—	V. sl.	150	Neut.	Nil.	Yell. pp.	Nil.	Wh. pp.	Buff pp.	Yell. pp.	Nil.

No.	SUBSTANCE.	HEAT.	HEAT c NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
242	Sucrose (CANE SUGAR)	M. to yell. liq. c. characteristic odor, ch. & vap. burns.	Br. & vap. burns.	Sl. yell. slowly.	Ch. almost at once.	Nil.	Nil.	160
243	Sulphonal ...	M. to wh. liq. c. a. pp. in it. Ch. gives cryst. sub. vap. burns c. sl. garlic odor.	Darkens sl. gives inflam. gas & sl. garlic odor.	Nil.	Red-br. & ch. quick.	Nil.	S.	126°
244	Terpineol ... (DISTILLATE FROM TERPINOL.)	Evaps. ent'ly, vap. burns.	Vap. burns.	Red-br.	Ch. v. quick.	Orange pink.	Nil.	—
245	Terpin Hydrate	M. evaps. c. inflam. vap. & wh. cryst. sub.	Vap. burns.	Yell. br.	Yell. to orange red & ch.	Orange pink.	Nil.	116
246	Tetra-Iodo-Pyrrol	Bl. & gives bl. sub. & vi. vap.	Alk. vap. goes gr.-grey to br.	Gr. Darkening slowly.	Light gr., turns dark then bl. c. vi. vap. & metallic sub.	Red br. slowly.	I. N.	—
247	Theobromine	M. to colorl'ss liq. sub. res. ch. c. alk. vap.	Bl. sl. c. strong alk. vap.	Nil.	Yell. but does not change.	Nil.	N.	Abt 300°



No.	SP. GR.	SOL. AQ. (1 in -).	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
242	—	Less than 0.5	Abt. 120	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
243	—	Sl.	50	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
244	0.944	Sl.	Misc.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Br pp.
245	—	Sl.	14	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
246	—	V. sl.	21	Neut.	Nil.	Nil.	Nil b. sl. red pp. a.	Nil.	Nil.	Nil.	V. sl.
247	—	V. sl.	Sl.	Neut.	Nil.	Nil.	Nil. b. v. sl. br. pp. a.	Nil.	Nil.	Nil.	Sl. red br. pp

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M Pt (°C)
248	<b>Theobromine Aceto Salicyl</b>	M. c. eff. to br. liq. wh. sub. acetous ch. and vap. burns.	Darkens sl. alk. vap. burns	Nil.	Dark red br., no ch.  Benzoic and Acetic odor.	Nil.	N.	—
249	<b>Theobromine Sodium Acetate</b>	Part m. & sl. wh. sub. ch. alk. vap.	Alk. vap.	Eff.	Yell. does not ch.	Eff.	N.	—
250	<b>Theobromin- Sod.-Salicyl</b>	Ch. Phenol odor, wh. dist. & alk. vap. burns.	Eff. str. alk. vap.	Nil.	Br. slowly, does not ch.	Nil.	N.	Nil
251	<b>Theophylline</b>	M. to yell. liq. sub. res. ch. and gives alk. vap.	Bl. sl. and alk. vap. burns.	Nil.	Yell. does not ch.	Nil.	N.	266
252	<b>Theophylline Sodium Acetate</b>	Part m. and ch. alk. vap. burns.	Alk. vap. burns.	Nil.	Yell. does not change.	Nil.	N.	—
253	<b>Thioresorcin</b>	Ch. yell. sub. & vap. burns.	Gr. then orange yell.	Gr. grey.	Dirty gr. & ch.	Eff. & goes dark br.	S.	—
254	<b>Thiosinamin</b>	M. to colorless liq. pun- gent garlic odor ch. alk. vap. burns.	Salmon col. chang- ing to yell. alk vap. burns.	Nil.	Yell. to red-br. & ch.	Nil.	N. & S.	74



No.	SP. GR.	SOL. AQ (1 in -)	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG.
248	—	Sl.	Sl.	Sl. ac.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
249	—	2	Sl.	Alk.	Lt. br. br. pp. b. & a.	Nil.	Nil.	Nil.	Nil.	Nil.	Yell. br. pp
250	—	2 (c.f. Vol. I.)	V. sl.	Str. alk.	Vi. col. b. vi. pp. a.	Wh. pp. rediss at first.	Nil.	Nil.	Br. color & v. sl. pp.	Nil.	Deep br. pp. turn- ing light- er.
251	—	S'.	90	Neut.	Nil.	Cryst. pp. v. slow- ly. Nil first.	Nil.	Nil.	Nil.	Nil.	Br. bl. pp.
252	—	20	Sl.	Str'ng alk.	Light br. pp. b. dark bl. pp. a.	Nil., red-br c. excess of Re- agent.	Nil. b. and a.	Nil.	Br. col.	Nil.	Dark br. pp.
253	—	V. sl.	V. sl.	Acid.	Nil b. sl. br. pp. a.	Nil.	Nil. b. sl. vi. br. pp. a.	Nil.	Nil.	Nil.	Nil.
254	—	18	2	Neut.	Red col. b., br. pp. a.	Yell. pp. rediss and giving wh. opal- es- cence.	Light blue pp. b., bl. pp. a.	Wh. pp.	Buff pp. rediss	Nil at first, sl. pp. a.	Or. yell. pp.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
255	Thymol	... M. evaps entirely aroma- tic vap. burns.	Pun- gent charac- teristic odor.	Nil.	Ch. slowly	Eff. & gives reddish oil.	Nil.	44
256	Thymol Iodide	M. to br. c. vi- br. vap. burns.	Goes bl.	Nil.	Vi. vap. & bl. sub.	Darkn's	I.	Nil.
257	Tiodin	... Ch. alk. vap. burns c. garlic odor	Eff. a lot, goes salmon pink and alk. vap. burns.	Br. bl.	Pinkish vi. c. vi. vap. br. dist. and garlic odor.	Br. bl.	N.S.I.	—
258	Toluol	... Evaps. entirely vap. burns.	Vap. burns.	Nil.	Br. and ch.	Nil.	Nil <sup>a</sup>	—
259	Tribrom- phenol	M. ch. gives wh. sub. and irritat- ing vap.	Ch.	Nil.	First m. and then ch. & c. br. irritat- ing vap.	Br. after a time.	Br.	85
260	Tribrom- phenol Bismuth	Bl. and gives yell. sub first & br. a.	Bl.	Turns grey.	First bl. and then br.	Red-br. c. sl. eff.	Br.	—
261	Tropacocaine HCl	M. ch. br. sub. half way up tube.	Wh. vap.	Eff. without ch.	Wh. fumes and ch.	Nil.	NCl.	—
262	Tylmarin	... M. ch. c. charact- eristic odor vap. burns.	Yell. c. eff. then color- less.	Gr. Yell.	Ch.	Yell.	Nil.	152



No.	SP. GR.	SOL. AQ. (1 in -).	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sub>2</sub> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG
255	—	1.500	0.375	Yell. pp.	Nil.	Wh. pp.	Nil.	Nil.	Nil.	Nil.	Nil.
256	—	Insol.	V. sl.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
257	—	Easily.	Misc.	Neut.	Nil b. sl. pp. a.	Br. pp.	Pale blue pp. b. cream pp. a.	Wh. pp.	Br. bl. pp.	Yell. pp. at first rediss	Red br. pp.
258	—	V. sl.	1	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
259	—	Insol.	3	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
260	—	Insol.	Insol.	Neut.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
261	—	2	About 9	Neut.	Red tinge	Yell. pp.	Nil.	Wh. pp.	Yell. p p	Yell. pp.	Red br. pp.
262	—	Sl.	15	Sl. ac.	Nil.	Sl. cloud.	Nil.	Nil.	Nil.	Nil.	Nil.

No.	SUBSTANCE.	HEAT.	HEAT c. NaOH.	H <sub>2</sub> SO <sub>4</sub> Cold.	H <sub>2</sub> SO <sub>4</sub> Hot.	HNO <sub>3</sub>	N.P.S. & Hal.	M. Pt. (°C)
263	Urea ...	M. gives wh. sub. & alk. vap. Res. goes solid & yell. then sub. en- tirely.	Strong alk. vap.	Nil.	Brisk eff. no col.	Nil.	N.	132
264	Urethane ...	M. evaps. vap. burns.	Alk. vap. burns.	Nil.	Dark br. not ch.	Nil.	N.	48
265	Veratrina ...	M. to yell. br. liq. Br. dist. vap. burns.	Br. & floats on soda.	Yell. to red slow.	Deep red & ch.	Pink to br.	N.	152
	Veronal, <i>see</i> Malo-Urea.							
266	Zinc Sulpho- Carb.	Ch. c. odor of Phenol. vap. burns.	Lique- fies.	Nil.	Ch. slowly.	Br. after a time.	S.	—



No.	SP. GR.	SOL. AQ. (1 in -).	SOL. ALC. (1 in -)	LIT- MUS.	Fe <sup>2+</sup> Cl <sub>6</sub> b. & a. boil.	BR. AQ.	FEH- LING'S b. & a. boil.	MAY- ER'S.	GOLD CHL.	ACID PIC- RIC.	DRAG
263	—	1	7½	Neut.	Nil.	Nil.	Nil b. sl. red pp. a.	Nil.	Nil.	Nil.	Nil.
264	—	2	Less than 1.	Neut.	Grey br. pp. b., dark br. pp. a.	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.
265	—	V. sl.	3	V. faint, alk.	Nil.	Yell. pp.	Nil.	V. sl. wh. pp.	Sl. cloud.	Nil.	Red br. pp.
266	—	2	3½	Sl. ac.	Vi. col. b. br. a	De- color- ised.	Wh. pp. re- diss. b. nil a.	Nil.	Nil.	Nil.	Nil.

## CORROBORATIVE TESTS.

1. **Acetanilide.**—Heated with Hydrochloric Acid or Potash Solution splits up into Anilin and Acetic Acid. Heated with Chloroform and Potash gives Phenyl-socyanide odor.

0.1 Gm. boiled with HCl 2 Cc. then mixed with 3 Cc. of Aqueous Phenol Solution (1 in 20) and 5 Cc. of filtered saturated Chlorinated Lime Solution, acquires brownish red color which changes to deep blue on adding Ammonia (Indophenol test U.S.P.)

Heated with Boric Acid over a naked flame, produces a yellow residue having a peculiar fragrant odour suggestive of sweet clover. Phenacetin will, under same conditions, produce the yellow colour. —Phenazone produces a pink colour and odour of Naphthalene. —Am. Jl. Ph., 1911, p. 269.

2. **Acetone.**—Oxidation with Bichromate and Sulphuric Acid gives Acetic and Formic Acids. Combines with Chloroform in presence of Caustic Alkali to form Acetone Chloroform  $(CH_3)_2$ :

$C \begin{cases} OH \\ CCl_3 \end{cases}$ , colorless crystals M.Pt.  $96^\circ C$ . insoluble in water. In aqueous solution can be thrown out by Salts, e.g., Calcium Chloride. For detection of small quantities, e.g., in urine by Iodoform Test, v p. 205.

3. **Acetophenone.**—With Hydroxylamin forms Acetoxim  $C_6H_5$  C(N.OH). $CH_3$  Colorless needles M.Pt.  $59^\circ C$ . This by action of Sulphuric Acid or Hydrochloric Acid in Glacial Acetic Acid solution is converted into Acetanilide (Beckmann's reaction).

5. **Acetyl-*p*-Amido-Salol.**—Yields Salicylic Acid on hydrolysis c. NaOH. Is not hydrolysed by HCl. Does not give Isonitrile test, but on adding the chloroform it gives a brownish red color.

When hydrolysing with dilute NaOH it turns blue, the color changing to reddish violet on boiling, the blue reappearing on cooling is changed to red with HCl.

7. **Acid. Acetyl-*o*-Coumaric**, see “Tyllmarin.”

8. **Acid. Agaric.**—Turns gelatinous and soapy on boiling with water and gives Pettenköfer's test, *c.f.*, Sodium Taurocholate.

11. **Acid. Carbol. Cryst.**—Turns brown with  $NaNO_2 + HCl$  and reddish brown on adding NaOH.

12. **Acid Cholalic.**—Gives blue unstable compounds with Iodine resembling Starch Iodide.—Watts *q.v.* for further full information.

13. **Acid Cinnamic.**—Oxidised with Potassium Permanganate to Benzaldehyde. Can be reduced by Sodium Amalgam to Hydrocinnamic Acid ( $\beta$ .phenyl-propionic Acid).

May be detected in presence of Benzoic Acid by suspending in 5% Uranium Acetate solution and exposing to sunlight,—in a few minutes odor of Benzaldehyde is evolved, and brown precipitate forms.—Allen.



15. **Acid Coumaric.**—Melted with KOH gives Salicylate and Acetate. Aqueous solutions of Alkaline Coumarates are fluorescent

16. **Acid Cresylic.**—Turns brownish with  $\text{NaNO}_2 + \text{HCl}$ , changing to reddish brown with NaOH.

17. **Acid Gallic.**—On adding Lime Water turbidity is produced, becoming grey green and darker.—Hager.

*Re Fehling's Solution Test*, Allen says reduces slowly and imperfectly.

Turns deep brown with  $\text{NaNO}_2$  alone.

19. **Acid Hippuric.**—Boiled with Acids or Caustic Alkalis decomposes into Benzoic Acid and Glycocoll.

20. **Acid Malic.**—Treated with Potash and Bromine Bromoform is formed.—Watts, q.v. *vide* also Schmidt.

22. **Acid Nucleinic.**—Schmidt II, 2, p. 1797, gives some information on the various Nucleinic Acids (animal, plant, yeast, etc.) but no very distinct analytical reactions. According to this authority Nucleinic Acids boiled with dilute Sulphuric Acid, their decomposition products yield Phosphoric Acid, Carbo-hydrates and Xanthin bases (Xanthin, Guanin, etc.). (Our tests were conducted with slightly brown Nucleinic Acid.)

23. **Acid Oleic.**—Characteristic odor. Solidifies at  $+4^\circ\text{C}$ . Pure Oleic Acid as such does not redden Litmus, but does, however, in Alcoholic Solution. Nitrous Acid converts it into the stereoisomeric Elaidic Acid in crystalline leaflets, M.Pt.  $45^\circ\text{C}$

24. **Acid Oxalic.**—A neutral alkaline salt Solution gives precipitate with soluble lime salt, insoluble in Acetic Acid, but soluble in HCl. Potassium Permanganate is decolorised in hot solution.

25. **Acid Pyrogallic.**—In presence of Caustic Alkali rapidly darkens, (Takes up Oxygen).

27. **Acid Sclerotic.**—Precipitated by Tannic Acid and Phosphomolybdic Acid.—Schmidt.

30. **Acid Tannic.**—Gives precipitate with gelatin,  $\text{Pb}(\text{NO}_3)_2$ ,  $\text{Bi}(\text{NO}_3)_3$  and Ammoniacal Copper Sulphate.—(Distinctions from Gallic Acid). Is hydrolysed into Gallic Acid by boiling with dilute Sulphuric Acid. Gives brown with  $\text{NaNO}_2$ .

34. **Acoine.**—Gives brownish green with  $\text{H}_2\text{SO}_4$  and  $\text{K}_2\text{Cr}_2\text{O}_7$ ; is precipitated both by acids and alkalies (Soluble 1 in 16,—P.J. i./10, 325: we found 1 in 30).

35. **Aconitine.**—There is no chemical identity test for; analyst has to rely on the sensation produced on the tongue in addition to the general characters stated.

36. **Adrenalin.**— $\text{NaNO}_2$  alone gives red color. For Phosphoretted Hydrogen odor with NaOH,—*vide* p. 131. Reduces  $\text{AgNO}_3$  Solution.

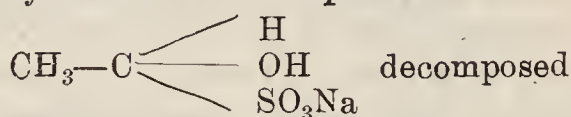
37. **Æsculin.**—Yields Glucose and Æsculetin on hydrolysis and then reduces Fehling's. Gives blood red color when treated with Nitric Acid and then excess of Ammonia. Gives blue fluorescence in alkaline solution. Treated with Sulphuric Acid and then solution of NaOCl gives violet color.—Allen, Watts.

38. **Æthyl Bromidum.**—Differs from the poisonous Ethylene Bromide by Sp. Gr. and boiling point.—*Vide* Vol. I., p. 800.

41. **Albumin Tannate.**—The Tannic Acid can be extracted by washing with water and alcohol. Nitrogen content 8%.—Schmidt, vol. II., 1, p. 1094 gives test for estimating its capabilities of withstanding Pepsin and Hydrochloric Acid.

42. **Alcohol Methylic.**—Method of detection in Ethyl Alcohol see p. 15.

43. **Aldehyde Absolute.**—Shaken with Concentrated Sodium Bisulphite Solution gives crystalline addition-product



by acid or alkali. Combines with Phenylhydrazin forming Ethyliden-phenylhydrazone. Combines with Ammonia, forming additive compound.

44. **Alloxan.**—Aqueous solution slowly turns red when applied to the skin. Solid NaOH turns spirituous solution blue, which is decolorised by water.

48. **Aloin.**—Ammonia changes an alcoholic solution of Barbaloin and Socaloin brown red, and Nataloin carmine red. Dieterich states the Aloins evaporated to dryness even in minute quantity with Nitric Acid (Sp. Gr. 1.4) on water bath, and the residue dissolved in alcohol, the red solution on adding a little Alcoholic KCN solution turns pink.

51. **Alypin.**—Behaves similarly to Cocaine, *c.f.*, p. 47. Can be distinguished by fact that 4% solution does not precipitate with Platinic Chloride in presence of HCl. (W.H.M.)

54. **Amyl Nitris.**—Characteristic odor,—produces flushing of face on inhalation,—for further information, *v.* Vol. I., p. 132, *et seq.*, and Vol. II., p. 19.

56. **Anaesthesin.**—Gives Isonitril reaction *c.f.*, Acetanilide.

57. **Anhydro-Glyco-Chloral.** Dilute Acids produce Chloral and Glucose.

58. **Anilin.**—A mixture of Nitric and Sulphuric Acids give fine blue color. To neutral aqueous or slightly alkaline solution add Sodium Hypochlorite or Chlorinated Lime Solution,—purple violet even in 1 in 26,000,—changing to dirty red. Avoid excess of Reagent (Runge). When this change has occurred add dilute Ammoniacal Phenol solution, return of blue color (Jacquemin-Dragendorff) even in 1 in 66,000. Aqueous Chromic Acid Solution according to concentration, gives green, blue, or almost black (Fritzsche). For other tests *vide* Schmidt or special Anilin Color treatises. Diazo test gives red dye.

59. **Anthrarobin.**—Easily soluble in Caustic Alkalis and Ammonia, giving yellowish solution gradually changing to green or blue owing to formation of Alizarin.



60. **Antimonii et Potassii Tartras.**—HCl Solution gives orange red pp. with  $H_2S$  soluble in Ammonium Sulphide and KOH. On "Marshing" black mirror insoluble in Sodium Hypochlorite Solution. With Lime Water white pp., soluble, when freshly precipitated, in Acetic Acid and Ammonium Chloride Solution.

65. **Apomorphine HCl.**—Solution in Sodium Hydrate rapidly becomes red and gradually black. Sodium Bicarbonate throws down precipitate which becomes green on standing.

Diazo test,—gives red color with  $HNO_2$  fading to brown and finally red color with  $\beta$ . Naphthol Soda.

66. **Arbutin.**—Hydrolysed by dilute Sulphuric Acid into Glucose and Hydroquinone. Diazo Test,—yellow with HCl and  $NaNO_2$  turning red with Sodium Hydrate.

69. **Argenti Proteinæ.**—Ammonium Sulphide colours solution blackish brown without causing pp. To 2 Cc. of Silver proteinate Solution (1 in 20) add 1 drop of 30% Acetic Acid, white caseous pp., soluble in excess.

Residue on incineration gives reactions for Silver. Picric Acid precipitates.—See also foreign pharmacopœias.

70. **Argonin.**—The results recorded in the chart were obtained with Argonin—*L*, the soluble preparation. Ammonium Sulphide turns solutions of it black without immediate precipitate.

72. **Arrhenal.**—See also XIVth Edition, *p.* 152.

73. **Arsamin.**—Diazo test gives positive reaction.—See also XIVth Edition, *pp.* 154 and 160.

74. **Asparagin.**—In alkaline solution is lævorotatory; in acid dextro. Copper Hydrate is dissolved on boiling, forming blue solution, depositing on cooling Asparagin-Copper  $(C_4H_7N_2O_3)_2Cu$ .

75. **Atropine Methyl Bromide.**—Gives Vitali's reaction *vide* Atropine.

76. **Atropine.**—1 mgr. warmed with 2 Cc. of 5% Mercuric Chloride in 50% Alcohol causes deposition of Mercuric Oxide (with some Mercurous)—Gerrard. Dilates the pupil even in 1 in 130,000 dilution. Responds to **Vitali's Reaction.**—On evaporating a trace of Atropine or one of its salts in a porcelain dish with a few drops of fuming Nitric Acid a yellowish residue is produced which on moistening with Alcoholic Potash (1 in 10) produces a violet colour. Strychnine does the same on applying a 4 per cent. potash solution, but the colour is evanescent. Veratrin produces a reddish violet or orange red colour. **Atropine Sulphate.**—Gives Atropine Gold Chloride.—M. Pt. 136–138°C.

77. **Benzol.**—To distinguish from Petroleum Benzin note solubility in Alcohol. Benzol is soluble with half its volume of Alcohol 90%, but Petroleum Benzin requires 5 to 6 times its volume (using 'Petrol' considerably more.—W.H.M.) 1 Cc. Petroleum Benzin added to 5 to 10 times the quantity of a mixture of 2 parts Nitric Acid (Commercial) and 1 part Sulphuric Acid,—warm

slightly :—Benzol gives with evolution of red vapors, yellow nitro compounds, then dilute with 10 to 15 times the quantity of water, odor resembling Bitter Almonds, especially on well diluting. Petroleum Benzin on this treatment is hardly affected. For Dragon's Blood Test, *vide* Vol. I., p. 274.

79. **Betaine HCl.**—Gold Salt melts at 224°C.

80. **Betol.**—Alcoholic Solution gives violet color with Ferric Chloride Solution.

82. **Bismuthi Citras.**—Soluble in  $\text{NH}_3$  and Alkali Citrates. Dissolved in Aqueous Ammonia and evaporated, Bismuth Ammonium Citrate is formed.

83. **Bismuthi Oxyiodogallas.**—Easily soluble in mineral Acids and Caustic Alkalis. Gradually turns red in moist atmosphere.

84. **Bismuthi Salicylas.**—For estimation of Salicylic Acid, *v. p.* 36.

85. **Bismuthi Subgallas.**—NaOH dissolves it with yellow color—turning red.

86. **Bromalhydrate.**—Decomposes at 100–110°C. into Bromal and water.

87. **Bromethylformine.**—Heated with Soda Solution gives odor of Formalin.

91. **Butyl Chloral.**—Nitric Acid converts it into Trichlorobutyric Acid, M.Pt. 44°C.

92. **Caffeine.**—Heated with Nitric Acid forms Cholestrophan.

94. **Caffeine Sodium Salicylate.**—Estimation of Caffeine can be conducted by extracting with boiling Chloroform.

97. **Camphor Monobromide.**—Alcoholic Potash has no action, but Silver Oxide in presence of Chloroform decomposes it. With Hydroxylamine, forms Camphor-Oxime  $\text{C}_{10}\text{H}_{16}=\text{N}-\text{OH}$ . M.Pt. 118°C. Heated with 4 times its quantity of Nitric Acid on sand bath forms Camphoric Acid and Brom-Nitro-Camphor. — Rhombic prisms almost insoluble in alcohol. M.Pt. 105° C.

98. **Cannabin Tannate.**—Shaken with Sodium Hydrate Solution and Ether, and the Ether Solution evaporated, a slightly alkaline yellowish residue (narcotic) remains.

99. **Cantharidin.**—Solubility in water 1 in 30,000 only. Boiled with Soda and Potash forms Cantharidates. 0.00014 Gm. of Cantharidin will produce a blister.—Schmidt.

102. **Chinolin.**—Diazo test gives slight brownish tinge. Boiling point 236–238°C. A mixture of Sulphuric Acid and fuming Nitric Acid produces crystallised Nitro-Chinolin  $\text{C}_9\text{H}_6\text{N}.\text{NO}_2$ . On water bath  $\text{H}_2\text{SO}_4$  produces mainly Cryst. *o*-Chinolin-Sulphonic Acid,  $\text{C}_9\text{H}_6\text{N}.\text{SO}_3\text{H}$ . The amorphous precipitate with Mayer's Reagent can be converted into amber yellow needles, on adding HCl.—Characteristic.—Allen.



103. **Chinosol.**—Diazo Test gives slight brownish red.

Mixture of *o*-Oxychinolin Sulphate and Potassium Sulphate. Former can be removed by Alcohol.—Schmidt, vol. II, 2, p. 1349.

104. **Chloralamid.**—Water slightly warm decomposes. Caustic alkalis decompose it into Chloroform, Ammonia and Alkali Formate. Dilute acids have no action on it.

105. **Chloral Hydrate.**—Warmed with a little strong NaOH Solution, Chloroform is liberated.

107. **Chrysarobin.**—Partially soluble in KOH Solution with red colour. Allen, 4th Edn., vol. V., p. 228, gives tests to distinguish Chrysophanic Acid from Chrysarobin. See also Hager, vol. I., p. 825.

M. Pts. of Commercial samples vary.

109. **Cinchonidine.**—Gives neither Thalleioquin Test nor the  $K_6Fe_2Cy_{12}$  Modification (*c.f.* Cinchonine). Soluble in large amount of Ether. Sodium Potassium Tartrate in neutral solution of a salt gives white precipitate.

110. **Cinchonine.**—Only slightly soluble in Ether (1 in 370). There are few characteristic reactions. Not precipitated by  $NaHCO_3$  in presence of Tartaric Acid (Quinine and Cinchonidine are). Does not give Thalleioquin Test, nor red color with  $K_6Fe_2Cy_{12}$  and Ammonia on addition of these to Acetic Acid Solution after treating with Br. (difference from Quinine and Quinidine). Not rendered fluorescent by very dilute Sulphuric Acid.

111. **Cinnamic Aldehyde.**—B. Pt. 245 to 247°. May be oxidised into Benzaldehyde and Benzoic Acid.

112. **Citrophen.**—M. Pt. 181° (Hager). Aqueous Solution is at first precipitated with NaOH Solution, then dissolved. Chromic Acid gives violet. Gives red color with Diazo reaction.

114 and 115. **Cocaine and Cocaine Hydrochloride.**—See p. 47 and Allen, 4th Edn., vol. VI., p. 322.

The identification of Cocaine and some Cocaine substitutes. Cocaine Salts and substitutes will react under certain conditions with Gold Chloride, Platinum Chloride, Chromic Acid and Potassium Permanganate to form precipitates which, when examined under the microscope, are found to possess definite and characteristic crystalline forms. The Alkaloid, isolated in the usual way, is converted into the Hydrochloride and made up to a 2% solution and tested under definite conditions.—Am. Jl. Ph. 1911, p. 195.

116. **Codeine Hydrochloride.**—Does not reduce Iodic Acid (Morphine does). No blue color with Ferricyanide and Ferric Chloride (Morphine gives)—*c.f.* Allen, 4th Edn., vol. VI., p. 392, 0.1 Gm. warmed with about 1 Cc. Sulphuric Acid and 1 drop of  $Fe_2Cl_6$  solution gives deep blue color.

Greenish blue with Fröhde's Reagent.

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117. **Colchicine**.—Only slightly soluble in Ether or Benzol. Practically insoluble in Petrol Ether.  $\text{H}_2\text{SO}_4$  with a trace of  $\text{HNO}_3$  added gives yellowish green changing to blue violet and wine red to yellow. (Dragendorff). Cl water gives yellow precipitate with an aqueous colchicine solution soluble in  $\text{NH}_3$  with orange color.—*c.f.* Allen, 4th Edn., vol. VII., p. 4.  $\text{NaNO}_2 + \text{HCl}$  give dirty brown pp.

119. **Conium Bases**.—See also p. 49.

120. **Cotarnin Hydrochloridum**.—Hager says 0.3 Gm dissolved in 4 to 5 Cc. water and Iodo-Potassic Iodide added, brown pp. formed which recrystallised from Alcohol melts sharply at  $142^\circ\text{C}$ .

121. **Cotarnin Phthalas**.—Can be split up into Cotarnine and Phthalic Acid.

126. **Cubebin**.—With  $\text{K}_2\text{Mn}_2\text{O}_8$  in alkaline solution oxidised to Piperonylic Acid and Oxalic Acid.—Schmidt, vol. II., 2, p. 1669.

127. **Dextrose**.— $[\alpha]_D = +104^\circ$  for the pure article in fresh solution. For the Hydrate  $[\alpha]_D = +90$  to  $96^\circ$ . Aqueous solutions of silver are reduced especially when warmed. In addition to Fehling's, Barfoed's Reagent (warm) is also reduced (distinction from Dextrin and Maltose). Sodium, Calcium and Barium Oxides form saccharates soluble in water. Ferments with yeast (useful confirmatory test).

128. **Dibromo-Tannin-Gelatin**.—Gives violet with dilute  $\text{NaOH}$ .

129. **Diacetyl Morphine**.—M. Pt.  $171^\circ\text{C}$ .  $\text{H}_2\text{SO}_4$  with a little  $\text{HNO}_3$  gives yellow red, darkening on warming. From Acid Solutions is precipitated by caustic alkalis, Ammonia and Ammon. Carb. redissolved by the the first in excess. Does not color Ferric Chloride blue or reduce Iodates (distinction from Morphine).

130. **Diacetyl Morphine HCl**.—Gives reactions of the base.

131. **Digitoxin**.—(See p. 52),  $\text{HCl}$  Sp. Gr. 1.19 dissolves it in the cold without coloration, but on warming it dissolves with brownish color.—*c.f.* Schmidt, vol. II., 2, p. 1640 for other special tests.

133. **Elaterin**.—With Fröhde's Reagent: first green then brown color. Mandelin's Reagent gives black, see also U.S.

134. **Emetine**.—Sulphomolybdic Acid gives brown color changed to blue by  $\text{HCl}$ . Chlorinated Lime Test *vide* Allen, 4th Edn., vol. VII., p. 42.

136. **Ephedrine base** melts at  $30^\circ\text{C}$ .—Schmidt. On oxidation yields Benzoic Acid, Oxalic Acid and Methylamine (Merck).

137. **Epicarin**.—Soluble in alkalis with red color. Alcoholic Solution gives with  $\text{Fe}_2\text{Cl}_6$  intense blue. Shaken with  $\text{KOH}$  and  $\text{CHCl}_3$  red color changing to brown on heating.—Hager. A drop of Concentrated Sulphuric Acid Solution turns green when exposed to the vapor of  $\text{HNO}_3$ .

A very dilute Solution in Concentrated Sulphuric Acid is green.



138. **Ergotinine**.—Anhydrous  $\text{Fe}_2\text{Cl}_6$  added to a solution in Concentrated  $\text{H}_2\text{SO}_4$  gives yellow color passing through orange, crimson and green to a permanent blue. A dilute Acetic Acid Solution layered on Conc.  $\text{H}_2\text{SO}_4$  gives an upper layer of violet and a lower one of green at junction of liquids.

140. **Ethyl-Morphine HCl**.—Does not give blue color with Ferric Chloride or reduce Iodates direct. 0.01 Gm. Dionine dissolved in 10 Cc. Sulphuric Acid after liberation of the HCl from the compound gives a clear solution which, on adding a drop of Ferric Chloride solution and warming turns violet to deep blue, changing to deep red on adding 2 to 3 drops of Nitric Acid. The free base (Ethyl Morphine) is less soluble in Ammonia than *Codeine*. Such solution reprecipitates the base in prismatic crystals melting at  $93^\circ\text{C}$ . Dionine is distinguished from *Morphine* in that, on adding t to a solution of Potassium Ferri-cyanide with Ferric Chloride, it does not give an immediate blue; but gradually a bluish green color.—Hager.

141. **Eucaïne Lactate** and **Eucaïne Hydrochloride**—1 drop of 1% Solution mixed with 1 drop of Mercuric Chloride Solution (1 in 20) gives no precipitate (difference from Cocaine).—P. Helv. This Pharmacopœia also gives an Ammonia precipitation test in several stages, *q.v.* Not colored by Fröhde's Reagent. 1 in 100 Solution gives no pp. with Potassium Iodide—Distinction from alpha-eucaïne—*Off*.

Moistened with  $\text{HNO}_3$  and evaporated to dryness and alcoholic KOH added—Benzoic Ether odor.—Hager.

A 4% solution of the hydrochloride gives slight golden brown pp. with Platinic Chloride dissolving in HCl and throwing out again crystalline after a few minutes.

142. **Eucalyptol**.—1 Cc. placed in a freezing mixture, and equal volume of Phosphoric Acid added gradually: a solid white crystalline mass of Cineol Phosphate results. If warm water be then added Cineol will separate.—U. S.

Agitated with strong solution of Iodine in Potassium Iodide a pasty mass is produced in which green lustrous crystals are formed.—Allen, 4th Edn., vol. IV., p. 285.

143. **Euresol**.—Gives reactions of Resorcin and Acetic Acid. On cautiously heating 0.05 Gm. with 0.1 Gm. Tartaric Acid and 10 drops of  $\text{H}_2\text{SO}_4$  a carmine red liquid is produced becoming pale yellow on diluting with water (Test for Resorcin.—U.S.). On heating 0.1 Gm. with 1 Cc. 5% KOH Solution and a drop of Chloroform crimson color results, changed to yellow by HCl (Test for Resorcin, U.S.).

144. **Euophen**.—Decomposed by water, Iodine being liberated also decomposed by alkalis.

145. **Exalgin**.—Characters similar to Acetanilide.

146. **Fluorescein**.—Unmistakable fluorescence. Heated with zinc dust and caustic soda reduced to colorless Fluorescin.

Extremely dilute solution shows green by reflected light and yellow by transmitted light. Color discharged by Acid.

147. **Formalin.**—Adds Ammonia. Reduces Ammoniacal Silver Nitrate Solution (Mirror). Responds to Schiff's Reagent. See also Milk Tests, Urine Tests and Paraform, *pp.* 271, 236, and Vol. I., p. 117.

148. **Fuchsin.**—Is decolorised by Zinc and HCl also by Sulphurous Acid. For detection of minute quantities as in urine, etc., see Schmidt, vol. II., 2, p. 1142, also p. 1771.

Diazo test destroys color,—dark brown with  $\beta$ . Naphthol.

Guaiacol gives dark reddish brown color with  $\text{NaNO}_2$  and HCl.

149. **Gelseminine.**—With  $\text{H}_2\text{SO}_4$  and  $\text{K}_2\text{Cr}_2\text{O}_7$  reddish violet then green.

151. **Glycogen.**—Iodine gives Burgundy red (Schmidt) O.R.,  $[\alpha_D] = +193.63$  (Huppert). Amorphous, readily soluble in alkalis.

154. **Guaiacol Carbonas.**—Hydrolised gives reactions for Guaiacol.

155. **Guaiacol Cinnamas.**—Hydrolised gives reactions for Guaiacol and Cinnamic Acid.

156. **Hexamethylene Tetramine.**—Boiled with dilute acids decomposes into Formaldehyde and  $\text{NH}_3$ .

157. **Holocain HCl.**—Yellow waxy pp. with  $\text{NaNO}_2$  and HCl.

158. **Homatropine (HBr).**—Dilatation of pupil which passes off rapidly in comparison with that produced by Atropine. Does not react to Vitali's test (Ac. Nitric Fuming, and Alcoholic KOH—*v.* Vol. 2, p. 447)—gives yellow instead of violet given by Atropine. Does not precipitate with Tannic Acid nor Platinic Chloride after previous addition of Hydrochloric Acid.

159. **Hydrastine.**—Fröhde's Reagent green to brown color. Vanadin Sulphuric Acid red to orange red. To distinguish from Hydrastinine, p. 71.

160. **Hydrastinine.**—The Sulphate dissolves with fluorescence.

161. **Hydrargyri Succinas.**—Easily Soluble in  $\text{HNO}_3$  on bringing together a fairly dilute solution of Alkali Succinate and the Mercury salt.

164. **Hyoscine HBr.**—Response to Vitali's reaction very similar to that with Hyoscyamine and Atropine.

165.—**Hyoscyamine Sulph.**—Reaction with Vitali's Test (Fuming Nitric Acid and Alcoholic KOH.) similar to that with Atropine. *q.v.* Gold Salt (recrystallised from hot water) is in golden shining leaflets, M.Pt. 160–163°C. Solutions reduce in the light.

Does not precipitate with Platinic Chloride Solution.—Difference from most Alkaloids—U.S.

166. **Hypnal.**—Gives green pp. with  $\text{NaNO}_2$  and HCl.

167. **Indigo.**—Purple vapors on heating in test tube. Color disappears on acting on it with Alkaline Reducing Agents, e.g., NaOH and Zinc, see also Schmidt, vol. II. 2, p. 1112 *et seq.*

168. **Indigo-Carmine.**—Diazo test gives green color.

170. **Iohydrin.**— $\text{NaNO}_2$  and HCl liberate Iodine.



171. **Lactophenin.**—Reacts similarly to Phenacetin with Chromic Acid Test.

172. **Lævulose.**—Reduces Bismuth Salts in alkaline solution). On warming with KOH or NaOH turns brown (as also Glucose). Fermentable direct, but more slowly than glucose. Lævorotatory.

173. **Lecithin.**—Boiled with Baryta gives Glycerophosphoric Acid, Neurine and a fatty acid (Stearic, Oleic or Palmitic).—Watts.

176. **Malourea, Syn., Veronal.**—A saturated solution acidified with Nitric Acid gives a white precipitate with Millon's Reagent, soluble in excess. This test is important from a forensic point of view.

*Toxicological Analysis* of Material for Veronal. The M. Pt.,  $191^{\circ}\text{C}$  is useful for identification. Substance must, of course, be pure. Viscera (take about 120 Gm.) are extracted with Alcohol and subsequently purified by Ether. N.B. 40 to 50% of the poison will probably have been excreted in the urine before death. Note that it gives no precipitate with the alkaloidal reagents; it is not decomposed by boiling with 20% Sodium Hydrate; it gives no brown color with Nessler's Reagent, but after fusing with Caustic Potash, cooling and then adding the Nessler Reagent, the usual brown coloration of ammoniacal bodies is formed. Veronal Solution treated with two drops of dilute Nitric Acid and then with Millon's Reagent gives a white gelatinous precipitate soluble in excess of the Reagent. W. H. Willcox.—L.ii/13,1179.

Veronal, detection of in stomach contents and urine. Fusion with Alcoholic Soda is the most characteristic.—W. Macadie, P.J. i/13,134.

177. **Mannitol Nitras.**—Explodes at  $120^{\circ}\text{C}$ .—Hager.

178. **Methylamino oxy-benzoas.**—Distinguished from Cocaine, Eucaine, Stovaine, Holocaine, Novocaine, Alypin and Tropococaine by Fröhde's Reagent, which gives a faint violet tinge, but nothing with the others except Tropococaine which gives slight green. Does not give Diazo reaction, but turns yellow with  $\text{NaNO}_2$  and HCl.

182. **Methylene Blue.**—Nitrous Acid converts it into Methylene green.

183. **Migralgin.**—Gives reactions of Phenazone, and Caffeine. The Citric Acid present is not easily detected—Solutions give no pp. with  $\text{CaCl}_2$ .

The Phenazone may be precipitated with Potassio-Mercuric Iodide (Caffeine is not precipitated). The presence of Antipyrin does not interfere with the Caffeine yielding the murexid reaction provided all the Phenazone precipitated with Br. Water is filtered out first.

If to a strong solution of Migralgin Ferric Chloride Solution be added in excess, then HCl, the red color is destroyed and a yellow pp. formed. Phenazone also gives this reaction.

Migralgin gives green color and pp. with  $\text{NaNO}_2$  and HCl.

184. **Morphine HCl.**—Reddish Violet quickly changing to Slatey Blue with Fröhde's Reagent. Liberates Iodine from Iodic Acid. Gives blue pp. with  $\text{Fe}_2\text{Cl}_6$  and  $\text{K}_6\text{Fe}_2(\text{CN})_{12}$ . Solution (freshly prepared).

186. **Nicotine.**—Dropped on paper causes a grease spot which disappears after a time. Phosphomolybdic Acid gives yellowish pp. For formation of Periodide (Roussin's crystals), see Hager, vol. II, p. 481.

187. **Nitrobenzene**.—Detection of traces: Distil with a little Sulphuric Acid in steam, shake distillate with Chloroform, convert. Oily drops into anilin by reduction with Zinc and Sulphuric Acid.

188. **Novocain**.—Diazo test gives red dye.—Note also distinctive colors in chart.

189. **Nuclein**.—c.f. Acid Nucleinic.

190. **Orexin Tannate**.—Gives Carbylamine reaction on heating with NaOH and  $\text{CHCl}_3$ . Turns resinous with dilute HCl. in the cold, but dissolves on heating.

191. **Paraform**.—Characteristic odor of Formalin on heating Distillate (Formalin collected in water) reduces Silver Nitrate (forming mirror). Responds to Schiff's Test (Sulphurous Fuchsin Solution). Sodium Nitroprusside 0.5% gives reddish color which on acidifying with Acetic Acid is changed to purple.

Nessler's Reagent gives a reddish precipitate which gradually changes to gray.—Schmidt.

If to 5 Cc Sulphuric Acid in which a little Salicylic Acid has been dissolved, 2 drops of Formalin Solution (37%) be added and the liquid very gently warmed, a permanent deep red color develops (U.S.). In general the distillate gives reactions of Aldehydes.

192. **Paraldehyde**—is more soluble in cold water than hot,—saturated aqueous solution becomes turbid on warming. Gives mirror with Ammoniacal Silver Nitrate Solution on warming (U.S.). Gives in general reactions of Aldehydes, but does not add Ammonia nor Sodium Bisulphite.

193. **Pelletierine**.—Process of extraction and characters of constituents.—Schmidt, vol., II., 2, p. 1582, *et seq.* **Pelletierine Tannate** turns brown at about  $150^\circ \text{C}$ . Softens at  $165^\circ \text{C}$ ., and decomposes without melting.—*Off.*

194. **Petroleum Ether**.—Does not dissolve Dragon's Blood (distinction from Benzene).

195. **Phenacetin**.—Potassium Dichromate in HCl Solution gives deep red colour, 1 Cc of a solution of 0.2 Gm. Phenacetin in 2 Cc HCl, (25%) boiled, cooled and filtered gives reddish violet on adding 5 drops of fresh Cl water.

196. **Phenalin**.—Alcoholic extractive evaporated to dryness gives reactions of Acetanilide.

197. **Phenazone**.—Gives green pp. with  $\text{HNO}_2$ .

Aqueous Solution gives with equal volume Nitric Acid yellow solution changing to crimson on warming. Tannin solution gives a white precipitate with a 1% solution.

199. **Phenazoni Salicylas**.—Green color with Sodium Nitrite and HCl.

200. **Phenocoll HCl**.—On treating 1 Cc of solution of 0.2 Gm. in 2 Cc of HCl (25%) boiled, cooled and filtered with 5 drops of fresh Cl water gives reddish violet color. 0.1 Gm. boiled with 2 Cc 33% NaOH and then 2 drops of  $\text{CHCl}_3$  added gives powerful Isonitrile odor and black oily drops float on surface.



202. **Phenolphthalein.**—Red color with caustic alkalis disappearing with Acids. Silver Nitrate gives violet pp.

203. **Phloridzin.**—Solutions have great avidity for Ammonia. In taking up 10% it turns to red and melts at the same time to a colorless mass. For details *re* Phloridzin-Ammonia see Schmidt, Vol. II., 2, p. 1715.

Mix 0.1 grm. with a crystal of Vanillin and 1 drop of HCl conc. and warm,—a fine red colour will result.

204. **Physostigmine.**—Calx Chlorinata turns a solution intensely red, but on further addition completely decolorises,—see also Schmidt for a number of other color reactions.

Brown color with  $\text{NaNO}_2$  and HCl turning blue with NaOH.

205. **Physostigmine Sulph.**—Brown color with  $\text{NaNO}_2$  and HCl, violet pp. with NaOH.

206. **Phytin.**—Solution throws down a pp. on heating. This is prevented by mineral acids, but not by Acetic.

Gives Reactions of Calcium and Mg. (Al. ?.)

207. **Picrotoxin.**—Mixed with 3 times its weight of  $\text{KNO}_3$  and then moistened with  $\text{H}_2\text{SO}_4$  and then NaOH in excess added gives intense red color.—Langley's Reaction.

To a trace on a watch glass add 1 drop 20% Benzaldehyde in absolute Alcohol and then 1 drop  $\text{H}_2\text{SO}_4$  without shaking,—violet color (Melzer),—see also Schmidt.

208. **Pilocarpine.**—To a solution in Conc.  $\text{H}_2\text{SO}_4$  add a trace of Potassium Bichromate,—bluish green immediately changing to fairly permanent green.

Phosphomolybdic Acid, Phospho-Tungstic Acid and Iodo-Potassic, Iodide pp. from HCl solution.

209. **Pilocarpine Nitrate** as Pilocarpine.

210. **Piperazin.**—Dissolves Uric Acid forming the neutral urate. Piperazin Phosphate forms 4-sided tabular crystals.

Gives white pp. with Nessler's Reagent.

Forms crystalline pp. with  $\text{NaNO}_2$  and HCl.

For further details, *vide* Allen, 4th Edn., vol. VII., p. 200.

211. **Piperazin Benzoate.**—Aqueous solution acidified with HCl throws out Benzoic Acid. The Aqueous Solution gives test for Piperazin *q.v.*

213. **Podophyllin.**—Podophyllotoxin constituent of, M.Pt.  $117^\circ\text{C}$ .

215. **Pyramidon.**—Gives violet colour with  $\text{NaNO}_2$  and HCl.

217. **Quinine Sulphate.**—Dissolves with blue fluorescence in  $\text{H}_2\text{SO}_4$ , Acetic Acid and Tartaric Acid. For substances interfering see Hager, p. 745.

Gives white pp. with  $\text{NH}_3$  soluble in Ether and in excess of  $\text{NH}_3$ . Thalleioquin Test with Cl and  $\text{NH}_3$ . See also Vol. I., p. 650.

The Thalleioquin Test is distinctive for Quinine and will show less than 0.0001 Gm. The presence of Belladonna, Colchicum, Conium, Gelsemium, Ipecacuanha, Opium, Nux Vomica do not inhibit the reaction at all. Work with dilute Solutions.—Am. Jl. Ph. Nov. 1912.

**218. Resorcin.**—On cautiously heating 0.05 Gm. with 0.1 Gm. Tartaric Acid and 10 drops Conc.  $\text{H}_2\text{SO}_4$  thick carmine red liquid produced which becomes yellow on diluting with water. Ammoniacal  $\text{AgNO}_3$  solution is reduced forming Mirror (*s.a.*)

Not precipitated by neutral Lead Acetate (distinction from Pyrocatechin),—see also Hager II., *p.* 724 for several further tests.

Gives brown pp. with  $\text{NaNO}_2$  and  $\text{HCl}$ .

Blue with  $\text{Fe}_2\text{Cl}_6$  changing to brownish yellow on adding  $\text{NH}_3$ : distinction from Catechol and Quinol.—U.S.

**219. Saccharin.**—Dissolved in 25%  $\text{KOH}$  *q.s.* and Br. water added till yellow coloration, Br. substitution body is gradually thrown out. Heated with Resorcin and  $\text{H}_2\text{SO}_4$  yellowish red then dark green color. After cooling dissolve the mass in water and add  $\text{NaOH}$  in excess,—intense green fluorescence (Bonstein says 0.0019 Gm. will give this).—Schmidt. See also U.S.

**220. Salacetol.**—Gives on alkaline hydrolysis reactions of Salicylic Acid and the hydrolysed liquid reduces Fehling's Solution, smells of Methyl Salicylate and burnt sugar and turns dark yellow.

**221. Salicin.**—Heated with Potassium Dichromate, a few drops of Sulphuric Acid and some water gives Salicylic Aldehyde (odor of Meadow Sweet).—Or dissolves in Hydrochloric Acid which on boiling throws out resin (Saliretin).

**222. Salicyl Salicylas.**—Yields Salicylic Acid on hydrolysis. Formula  $\text{C}_6\text{H}_4.\text{OHCOO}.\text{C}_6\text{H}_4\text{COOH}$ , *i.e.*, Salicyl-Salicylic Acid.

**223. Sal Limonis.**—Calcium Chloride gives white pp., insoluble in Acetic Acid. Potash flame. Decolorises  $\text{K}_2\text{Mn}_2\text{O}_8$  with effervescence on warming at 60-65° with Ac. Sulph. dil.

**225. Salol.**—Alcoholic Solution precipitates with Bromine. Violet with Ferric Chloride in alcoholic solution. Test for Phenol and Salicylic Acid after melting with Soda.

**226. Saloquinine.**—On hydrolysis gives reactions of Quinine and Salicylic Acid.

**228. Santalol Salicylas.**—Alcoholic solution colored violet by  $\text{FeCl}_3$  solution.

**232. Sodium Glycerophosphate.**—On incineration Pyrophosphate is formed.

Lead Acetate precipitates but not Magnesia mixture. Cold Ammonium Molybdate, either precipitates on standing or heating.

**233. Sodium p-aminophenylarsonate.**—See also *p.* 26, and previous Edition for further analytical information.

**235. Sodium Sulphocarbolate.**—Dilute solution does not give yellowish brown with Uranium Nitrate solution (distinction from Salicylate), Soda flame.

**237. Sodium Taurocholate.**—Taurocholic Acid forms shining hygroscopic bitter needles easily soluble in water and alcohol. Solutions dextrorotatory. On heating with water at 100° C. or boiling with  $\text{KOH}$  or acids, decomposes into Cholic Acid  $\text{C}_{24}\text{H}_{40}\text{O}_5$  and Taurin  $\text{C}_2\text{H}_7\text{NO}_3\text{S}$ .—Watts and Schmidt.



To Aqueous Solution of the Sodium Salt add  $\frac{2}{3}$  bulk of Sulphuric Acid and a few drops of Syrup. Intense violet color develops.—Pettenköfer's Bile Acid Test.

**238. Sparteine Sulphate.**—For further tests *vide* U.S., and Ammonium Sulphydrate forms permanent orange red color.

New Sparteine Test Reaction.—P.J. ii./II, 463.—ex Journ. de Pharm. Chim. Sept. 1/II, p. 25.

**240. Strophanthin.**—Re the  $\text{FeCl}_3$  test—add a trace of  $\text{FeCl}_3$  to an aqueous solution, then Concentrated Sulphuric Acid to obtain brownish pp. which changes in two hours to dark green.—Schmidt.

Solution dextrorotatory.—(U.S.)

**241. Strychnine.**—Gives Violet with  $\text{K}_2\text{Cr}_2\text{O}_7$  and  $\text{H}_2\text{SO}_4$ , and a yellow passing into reddish violet with Vitali's Reaction *v.* p. 447.

Mandelin's Reagent gives blue color changing to vermillion. On adding alkali a permanent pink to purple color results.

Phospho-molybdic Acid will show 0.0001 Gm., Picric Acid 0.00005 Gm., Tannic Acid 0.00004 Gm., Mercuric Potassium Iodide 0.000006 Gm., Potassium Bismuth Iodide 0.00002 Gm., Platinic Chloride only 0.001 Gm., and Gold Chloride 0.0001 Gm.—Dragendorff.

**242. Sucrose.**—Conc. KOH turns this brown on *heating*. (Glucose is turned brown in the *cold*.) It is not directly fermentable—requires inversion first by yeast or dilute acids into glucose and laevulose. See also U.S.

**244. Terpeneol.**—B. Pt. 218-219°.—See Schmidt, vol. II., 2, p. 1187.

**245. Terpin Hydrate.**—Conc. HI converts into  $\text{C}_{10}\text{H}_{16}2\text{HI}$ , see also U.S. and Schmidt, vol. II., , p. 1186.

**246. Tetra-Iodo-Pyrrol.**—Warmed with  $\text{NaOH}$  and Zinc filings, fumes of Pyrrol are given off. These color pine wood, *e.g.*, a match soaked in HCl bright red. Gives bright red on warming an alcoholic solution with Nitric Acid (Allen).

**247. Theobromine** gives Murexid Test. Precipitates Silver Theobromine on adding  $\text{AgNO}_3$  Solution to very dilute Solution of Theobromine Nitrate. Sodium phospho-tungstate gives yellow pp. Treated with dilute  $\text{H}_2\text{SO}_4$  and Lead Dioxide  $\text{CO}_2$  is evolved. Product precipitates Sulphur from  $\text{H}_2\text{S}$ , colors skin purple red and turns blue with moderate amount of Magnesia.

**249. Theobromine Sodium Acetate.**—Gives murexid reaction. Aqueous solution 1 in 5 neutralised with dilute Hydrochloric Acid in presence of Litmus Solution gives white precipitate of Theobromine. (A little alkali assists its solubility in water).

**250. Theobromine-Sodium Salicylate.**

On acidifying with Hydrochloric Acid, Salicylic Acid is thrown out which may be identified. Theobromine may be removed from filtrate with Chloroform, this will give the Murexide Reaction.

**251. Theophylline.**—Gives Murexid Reaction.

252. **Theophylline Sodium Acetate.**—Gives reactions of Theophylline and also of Acetate (after removing the Theophyllin by neutralising and filtering).

254. **Thiosinamin.**—For conversion into Allyl Cyanamide see Schmidt, vol. II., 1, p. 772.

$\text{NaNO}_2$  and  $\text{HCl}$  pp. yellow oil with mustard odor.

257. **Tiodine.**—Contains Thiosinamin *q.v.*

$\text{NaNO}_2$  and  $\text{HCl}$  gives brown pp. turning yellow with  $\text{Na}$  hthol.

Yellow pp. with  $\text{Pb. Acet.}$ , insoluble in dilute  $\text{HNO}_3$ , but blackened by conc.  $\text{HNO}_3$ .

258. **Toluol.**—Sp. Gr. 0.872 at  $15^\circ\text{C}$ . Yields Benzoic Acid on oxidation.

260. **Tribromphenol Bismuth.**—Gives Bismuth Reaction<sup>s</sup> using an acidulated extractive.

261. **Tropacocaine HCl.**—Boiled with  $\text{HCl}$  converted into Benzoic Acid and pseudo-tropine.

262. **Tylmarin.**—Soluble in Chloroform 1 in 14 (distinction from Acid Coumaric, which is only very slightly soluble).

263. **Urea.**—Gives Biuret Reaction. Decomposes with Hypobromite (*vide pp. 83, 213, 249*).

264. **Urethane.**—M. pt.  $50^\circ$  (we find considerably more soluble than published statement).

265. **Veratrine.**—Gives Vitali's Reaction *q.v.*

266. **Zinc Sulphocarbolate.**—Yellowish green pp. with  $\text{Pot. Ferro-cyanide}$  insoluble in  $\text{HCl}$  (method of distinction of Zinc from Aluminium in analysis).

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# Approximate Melting Points and Consistence (*Atmospheric Temperature, 11°C*) of some Fats and Waxes suitable for Suppositories, Pastes, Creams and Ointments.

	31-32° C.	87·8-89·6° F.	
Oleum Theobromatis			Yellowish white, hard, brittle, and melts with ease.
Sevum Preparatum	39	102·2	Rather hard and brittle, but melts with ease.
Oleum Theobromatis } partes æq.			{ Stiff paste. Easily softened with the fingers. Suitable for thick creams.
Paraffinum Molle } partes æq.			
Oleum Theobromatis	33-34	91·4-93·2	
Paraffinum Molle	35-39	95-102·2	
Unguentum Cetacei, ( <i>Off.</i> )	35	95	White, soft base.
Adeps	38	100·4	Soft, white, unctuous.
Japan Wax	50	122	Hard, tough, and tenacious, tallowy. Obtained from <i>Rhus</i> species.
Adeps Lanae	40-44	104-111·2	Yellowish, stiff, tenacious, unctuous.
Oleum Theobromatis } partes æq.			{ Hard. Melts easily between the fingers. Not so brittle as Oleum Theobromatis.
Cetaceum	39-40	102·2-104	
Sevum Preparatum	47	116·6	Soft and unctuous.
Cetaceum	46-50	114·8-122	Crystalline, scaly and slippery.
Unguentum Paraffini, ( <i>Off.</i> )	47	116·6	Stiff unguent.
Ceresin } partes æq.			Very hard white mass.
Stearin }			
Cera Alba 1, Oleum Theobromatis 6	51-52	123·8-125·6	Hard glossy mass. Easily melts between the fingers.
Japan Wax, Hard Paraffin, equal parts	48-51	118·4-123·8	Hard, white and brittle.
Ceresin	52-53	125·6-127·4	Hard, like good paraffin.
Stearin	53-54	127·4-129·2	White, hard, crumbling substance.
Paraffinum Durum	54-57	129·2-134·6	Crystalline, hard and unctuous (slightly greasy).
Unguentum Resinæ, ( <i>Off.</i> )	54	129·2	Stiff white pomade.
Adeps 3 with Sera Alba 1	59	138-2	Very hard, white mass.
Adeps, Cera Alba, equal parts	58	136·4	Hard as last, but not so white in appearance.
Cetaceum, Cera Alba, equal parts	58-59	136·4-138·2	White, hard, tenacious
Cera Alba	62-64	143·6-147·2	Hard, yellowish, from leaf buds of <i>Copernicus cerifera</i> .
Carnauba Wax	85	185	Stiff mass, melting easily.
Carnauba Wax 1, Oleum Amygdalæ 4	77-78	170-6-172·4	Stiff ointment of brownish colour.
Carnauba Wax 1, Oleum Amygdalæ 3	78-79	172·4-174·2	
Cera Alba, Oleum Amygdalæ, equal parts	60-61	140-141·8	Hard and wax-like.
Cera Alba 1, Oleum Amygdalæ 5	54	129·2	Stiff ointment.
Cera Alba 1, Oleum Amygdalæ 9	52-53	125·6-127·4	Stiff ointment base.
Cera Alba 1, Oleum Amygdalæ 19	48-49	118·4-120·2	{ Very soft creams.
Cera Alba 1, Oleum Amygdalæ 39	43	109·4	

## FREEZING MIXTURES.

For cooling and setting suppositories, bougies, &amp;c.

The following is a list of some freezing mixtures best prepared from commercial Crystalline Salts, and in a thick wooden vessel:—

	Temp. F. reached.
Ammonium Nitrate 1, Water 1 .. .. .	+ 1'4
Sodium Nitrate 3, Dilute Nitric Acid 2 .. .. .	— 3
Ice 2, Sodium Chloride 1 .. .. .	— 5
Ammonium Nitrate 1, Sodium Carbonate 1, Water 1 .. .. .	— 7
Ice 24, Sodium Chloride 5, Ammonium Nitrate 5 .. .. .	— 18
Ice 3, Sulphuric Acid 2 .. .. .	— 23
Ice 8, Hydrochloric Acid 5 .. .. .	— 27
Ice 3, Dilute Nitric Acid 2 .. .. .	— 46
Sodium Phosphate 3, Ammonium Nitrate 2, Dilute Mixed Acids 4 .. .. .	— 50
Ice 8, Dilute Sulphuric Acid 10 .. .. .	— 91



## DROP MEASURE TABLE.

Showing the number of drops per gramme from various medicaments delivered (at 15° C.) by a standard pipette 3 mm. in external diameter (see 'Weights and Measures'). Adapted from F.E.

	No. of drops in 1 Gm.
Acetum Opii Compositum .. .. .	54
Acidum Hydrochloricum (1'171) .. .. .	21
„ Hydrocyanicum Dilutum (2%) .. .. .	22
„ Nitricum, Sp. Gr. 1.321 .. .. .	25
„ Phosphoricum, Sp. Gr. 1'35 (50% H <sub>3</sub> PO <sub>4</sub> ) .. .. .	19
„ Sulphuricum, Sp. Gr. 1'843 .. .. .	26
„ Sulphuricum Alcoholisatum (Aqua Rabeliana) (Sulphuric Acid 1, Alcohol 3) (cautiously mixed) .. .. .	55
„ Sulphuricum Dilutum 10% .. .. .	21
Æther .. .. .	91
„ Aceticus, Sp. Gr. 0'915 .. .. .	60
„ Sulphuricus Alcoholisatus (Hoffman's Anodyne) (Ether 4 and Alcohol 1, mixed) .. .. .	73
Aqua Distillata .. .. .	20
Chloroformum, Sp. Gr. 1'48 .. .. .	60
Creosotum, Sp. Gr. 1'08 .. .. .	42
Liquor Ammoniae, Sp. Gr. 0'923 .. .. .	24
Oleum Crotonis Tiglii (Aceite de Croton Tiglio) .. .. .	44
„ Menthae Piperitæ, Sp. Gr. 0'89 to 0'92 .. .. .	52
„ Terebinthinæ .. .. .	56
Solutum Chloruri Ferrici, Sp. Gr. 1'26 (Liquor Ferri Perchloridi) .. .. .	18
Tinctura Alcoholica Aconiti (1 of Root in 10) .. .. .	58
„ „ Belladonnæ, 1 in 10 .. .. .	59
„ „ Cantharidis, 1 in 10 (with Cochineal 1.5 in 100) .. .. .	58
„ „ Castorei, 1 in 20 .. .. .	57
„ „ Colchici, 1 in 10 .. .. .	59
„ „ Corticis Aurantii (Naranja) Composita (Tinctura Roborans ex Whytt) .. .. .	63
„ „ Digitalis, 1 in 10 .. .. .	58
„ „ Fabæ Sancti (Haba de San Ignacio) (Ignatii Composita) Guttæ Amaræ ex Baumé 1 in 2 .. .. .	58
„ „ Hamamelidis (bark and leaves of each, 1 in 20) .. .. .	58
„ „ Hydrastis, 1 in 10 .. .. .	58
„ „ Iodi (1 in 10, Alcohol 95%) (Solucion Alcohólica de Yodo) .. .. .	62
„ „ Lobeliæ, 1 in 10 .. .. .	58
„ „ Moschi (Almizcle) 1 in 25 .. .. .	55
„ „ Nucis Vomicae, 1 in 10, 0'25% Alkaloids approxi- mately .. .. .	57
„ „ Opii (Extract, 1 in 20) .. .. .	58
„ „ Scillæ (escila) 1 in 5 .. .. .	58
„ „ Strophanthi (Estrofanto) 1 in 10 .. .. .	58
„ „ Viburni, 1 in 10 .. .. .	58
(all the above tinctures are made with Alcohol 70%).	
Opii Compositum (Laudanum ex Sydenham) .. .. .	40

# GLOSSARIES

OF WORDS AND PHRASES LIKELY TO OCCUR AS DIRECTIONS IN  
FOREIGN PRESCRIPTIONS.

## DANISH GLOSSARY.

- Aandedrag*, breathing.  
*Aare*, vein.  
*Aare-Indsprøjtning*, intravenous injection.  
*Atomsprøjte*, spray or atomiser.  
*Badevand*, lotion (lit. bath water).  
*Badning*, fomentation.  
*Blære*, blister.  
*Blandes*, to be mixed.  
*Belægges (Piller)*, to be coated (pills).  
*Børstes*, to be brushed.  
*Brækmiddel*, emetic.  
*Citronsaft*, lemon juice.  
*Daglig*, daily.  
*Den smærtefulde Del*, the painful part.  
*Dessertskefuld*, dessertspoonful.  
*Draaber*, drops.  
*Døgnet*, the space of 24 hours.  
*Efter Maaltid*, after meals.  
*Etiket med Anvisning*, label with formula.  
*Flaske*, bottle.  
*Forkølelse*, cold.  
*Forsølves (Piller)* to be coated (pills).  
*Fortyndes*, to be diluted.  
*For udvortes Brug*, for external use.  
*Før Maaltid*, before meals.  
*Gift*, poison.  
*Glas Kapsler eller smaa Flasker* glass capsules or ampoules.  
*Glasstang*, glass rod.  
*Gnidning*, friction.  
*Gummerne*, the gums.  
*Gurglevand*, gargle.  
*Haarvand*, hair-lotion.  
*Hjerte*, heart.  
*Hostemixtur*, cough-mixture.  
*Hovedpine*, head-ache.  
*Hud-Indsprøjtning*, subcutaneous.  
*Hver anden*, every two.  
*Hver tredje*, every three.  
*Igle*, leech.  
*Ikke*, not.  
*I lige Dele*, of each equal parts.  
*Indaanding-indaader*, inhalation-inhaler.  
*Indgnid*, rub.  
*Indgnides*, to be rubbed.  
*Indgydes*, to be instilled.  
*Indsprøjtjes*, to be injected.  
*Indsprøjtning*, injection.  
*I Vægt*, by weight.  
*Klystér*, enema.  
*Knuses eller brækkes*, to be crushed or broken.  
*Kop*, cup.  
*Krukke*, pot.  
*Latverge*, electuary.  
*Lige Dele*, equal parts.  
*Ligtorn*, corn.  
*Mælk*, milk.  
*Mellem*, between.  
*Moderkrans*, pessary.  
*Mundvand*, mouth-wash.  
*Muskel-Indsprøjtning*, intramuscular injection.  
*Nat*, night.  
*Næse*, nose.  
*Næsebor*, nostrils.  
*Omrystes*, shake (the bottle).  
*Omslag*, poultice.  
*Ophlæsning*, flatulence.  
*Opløse*, dissolve.  
*Opsnuses gennem Næseborene*, to be sniffed up the nostrils.  
*Pensle*, paint (lit. pencil).  
*Pensles*, to be painted.  
*Rystes*, shake (the bottle).  
*Signatur*, label (medical label).  
*Skefuld*, spoonful.  
*Smærte*, pain.  
*Som foreskrevet*, as directed.  
*Spiseskefuld*, tablespoonful.  
*Sprøjte*, syringe.  
*Stikpille*, suppository.  
*Straks*, at once.  
*Tages*, to be taken.  
*Tandmiddel*, dentifrice.  
*Teskefuld*, teaspoonful.  
*To Gange*, twice.  
*Tre Gange*, three times.  
*Ved Sengetid*, just before retiring to rest (lit. at bed-time).  
*Vekselvis*, alternately.  
*Vægt*, weight.  
*Øjendraaber*, eye-drops.  
*Øjelaag*, eye-lids.  
*Øjenhaar*, eye-lashes.  
*Øjenskaerm*, eye-shade.  
*Øjenvand*, eye-wash.  
*Ørepine*, ear-ache.



**DUTCH GLOSSARY:**

*Ademhaling*, breathing.  
*Ader*, vein.  
*Bedekken (pillen)*, to be coated (pills).  
*Besproeiingstoestel*, atomiser or spray.  
*Bestrijken*, to be painted.  
*Blaar*, blister.  
*Baarmoederkrans*, pessary.  
*Braking*, vomiting.  
*Citroensap*, lemon juice.  
*Dagelijks*, daily..  
*De flesch*, bottle.  
*Dicht bij*, near to.  
*Den volgende morgen*, the next, or following morning.  
*Droppels or druppels*, drops.  
*Etiket met recept*, label with formula.  
*Gebruik*, use, application.  
*Gedurende het bruisen*, during effervescence.  
*Gegruisd of in stukjes gebroken*, to be crushed or broken.  
*Gelijke deelen*, equal parts.  
*Glazen capsules*, glass capsules or ampoules.  
*Glazen staafje*, glass rod.  
*Goedschudden*, to be well shaken (the bottle).  
*Gorgelen*, gargle.  
*Het pijnlijk deel*, the painful part.  
*Het tandvleesch*, the gums.  
*Hoest, de*, the cough.  
*Inademing-respirateur* Inhalation-inhaler.  
*Indien het hoesten lastig is*, when the cough is troublesome.  
*Indruppelen*, to be instilled.  
*Inspuiting binnen de spieren*, intramuscular injection.  
*Inspuiting binnen de aderen*, intravenous injection.  
*Inspuiting onder de huid*, subcutaneous injection.  
*Klisteerspuit*, enema.  
*Kokend*, boiling.  
*Kopje*, cup.  
*Melk*, milk.  
*Met mate*, moderately.  
*Mondspoeling*, mouth-wash.

*Na den maaltijd*, after meals.  
*Neerliggende (rustende)*, lying down.  
*Niet te gebruiken*, not to be taken.  
*Om de beurt*, alternately.  
*Om op te snuiven*, to be sniffed up the nostrils.  
*Onmiddellijk*, immediately.  
*Ooghaartjes*, eye-lashes.  
*Oogkapje*, eye-shade.  
*Oogleden* eye-lids.  
*Oogwassching*, eye-wash.  
*Ook*, also.  
*Op de gebruikelijke wijze*, in the usual manner (as taken before).  
*Papmiddel*, fomentation.  
*Per gewicht*, by weight.  
*Plaatselijk aan te wenden*, for local use only.  
*Potje*, pot.  
*Prikkelend*, irritable.  
*Purgeerend stroopje*, electuary.  
*Spoeling voor de oogen*, eye-wash.  
*Steekpilletje*, suppository.  
*Sproeier*, spray.  
*Spuit*, syringe.  
*Stopsel van pluksel*, tampon.  
*Tabletje*, tablet.  
*Tandpoeder*, dentifrice.  
*Van elk evenveel*, of each equal parts.  
*Verdeeld in gelijke deelen*, let it be divided into equal parts.  
*Vergift*, poison.  
*Verzilveren (pillen)*, to be silvered (pills).  
*Volgens het voorschrift*, as directed.  
*Voor het naar bed gaan*, just before retiring to rest.  
*Voor inspuiting*, to be injected.  
*Voor inwendig gebruik*, for internal use.  
*Voor uitwendig gebruik*, for external use.  
*Waskaars*, bougie.  
*Winderigheid*, flatulence.  
*Wrijven*, rub.  
*Wrijving*, friction.  
*Zonder*, without.  
*Zoo noodig*, if necessary.

**FRENCH GLOSSARY.**

*A argenter (pilules)*, to be silvered (pills).  
*A broyer ou concasser*, to be crushed or broken.  
*A dragéifier (pilules)*, to be coated (pills).  
*A être instillé*, to be instilled.  
*A moins que*, unless.  
*Ampoule*, blister.  
*Après les repas*, after meals.  
*Au-dessus*, above.  
*Au poids*, by weight.  
*Baguette en verre*, glass rod.

*Bien*, well.  
*Bien agiter le flacon*, the bottle to be well shaken.  
*Boire*, drink.  
*Bouillant*, boiling.  
*Chaque jour*, daily.  
*Charpie*, lint.  
*Chauffé*, warmed.  
*Cils*, eye-lashes.  
*Coeur (le)*, the heart.  
*Collyre*, eye-wash.  
*Comme il a été prescrit*, as directed.  
*Coton hydrophile*, absorbent wool.

**French Glossary—continued.**

*Crépine et pulvérisateur*, spray and atomiser.  
*Cuillerée*, spoonful.  
*Cuillerée à dessert*, dessert-spoonful (10 gm.).  
*Cuillerée à thé*, teaspoonful (*ou à café*—5 gm.).  
*Cuillerée ordinaire*, tablespoonful (15 gm.).  
*Cuir*, leather.  
*De bonne heure demain*, early to-morrow.  
*De jour en jour*, from day to day.  
*De la façon habituelle*, in the usual manner.  
*De la façon prescrite*, in the manner directed.  
*Demain matin*, to-morrow morning.  
*Demain soir*, to-morrow night.  
*De temps en temps*, occasionally.  
*Dissoudre*, dissolve.  
*Douleur*, pain.  
*Droite (à)*, to the right.  
*Enème*, enema.  
*En se couchant*, lying down.  
*Ensemble*, together.  
*Entre* between.  
*Etiquette*, slip-label.  
*Etiquette avec formule*, label with formula.  
*Flacon*, bottle.  
*Flacon (le) ayant été agité*, the bottle having been shaken.  
*Flatuosité*, flatulence.  
*Fomentation*, fomentation.  
*Garde-vue*, eye-shade.  
*Gargariser*, gargle.  
*Gencives (les)*, the gums.  
*Hier*, yesterday.  
*Inhalation-inhalateur*, inhalation-inhaler.  
*Injecteur*, syringe.  
*Injection intramusculaire*, intramuscular injection.  
*Injection intraveineuse*, intravenous injection.  
*Jus de citron*, lemon juice.  
*Jusqu'à ce que*, up to.  
*Juste avant d'aller se coucher*, just before retiring to rest.  
*La hanche*, the hip.  
*Lait*, milk.  
*Main (la)*, the hand.

*Le (or la) même*, the same.  
*Ne pas avaler*, not to be taken.  
*Nuit*, night.  
*Par degrés*, by degrees.  
*Paupières*, eye-lids.  
*Pendant l'effervescence*, during effervescence.  
*Pendant que la douleur dure*, while the pain lasts.  
*Poignée*, handful.  
*Pour être appliqué avec la brosse*, to be brushed.  
*Pour être appliqué avec le pinceau*, to be painted.  
*Pour être aspiré par les narines en renflant*, to be sniffed up the nostrils.  
*Pour être injecté*, to be injected.  
*Pour l'usage partiel seulement*, for local use only.  
*Pour placer dans l'oeil*, to be placed in the eye.  
*Pour usage extérieur*, for external use.  
*Près de*, near to.  
*Quand la toux est gênante*, when the cough is troublesome.  
*Rince-bouche*, mouth wash.  
*Sangsue*, leech.  
*Sans*, without.  
*Semaine*, week.  
*Seul*, e, alone.  
*Si nécessaire*, if necessary.  
*Tasse*, cup.  
*Tous les deux jours*, every other day.  
*Tout les matins (soirs)*, every morning (night).  
*Tous les quarts d'heure*, every quarter hour.  
*Tous les trois jours*, every third day.  
*Toutes les deux heures*, every two hours, or every other hour.  
*Tout (la)*, the cough.  
*Un blanc d'oeuf*, white of an egg.  
*Une fois*, once.  
*Un jaune d'oeuf*, yolk of an egg.  
*Veine*, vein.  
*Verre à madère*, wineglass.  
*Verrée (une)*, wineglass (8 cuillerées ordinaires—20 gm.).  
*Versez*, pour off.

**GERMAN GLOSSARY.**

*Abend*, evening.  
*Abkochung*, decoction.  
*Abwechselnd*, alternately.  
*Ader*, vein.  
*Alle-Stunden-Tropfen zu nehmen*, so many drops every - hours.  
*Alle viertel Stunden*, every quarter-hour.  
*Alle zwei Stunden*, every other hour.

*Allmählich*, by degrees.  
*Anwenden*, apply.  
*Atmen*, breathing.  
*Auflösen*, dissolve.  
*Augenlider*, eye-lids.  
*Augenschirm*, eye-shade.  
*Augenwasser*, eye-wash.  
*Augenwimpern*, eye-lashes.  
*Ausgenommen wenn*, unless



## German Glossary—continued.

- Ausgiessen*, pour off.  
*Äusserlich anzuwenden* for external use.  
*Bähung*, fomentation.  
*Becher*, a cup.  
*Beim zu Bett gehen*, at bedtime.  
*Bis auf*, up to.  
*Blähung*, flatulence.  
*Blutegel*, leech.  
*Brandblase*, blister.  
*Bürsten*, to be brushed.  
*Charpie-Bausch*, tampon.  
*Der schmerzende Teil*, the painful part.  
*Dasselbe*, the same.  
*Dessertlöffel*, dessertspoonful.  
*Diese Arznei darf nicht eingenommen werden*, not to be taken.  
*Diese Arznei darf ohne erneute schriftliche Verordnung des Arztes nicht repetiert werden*, this medicine may not be repeated without written order of the physician.  
*Dragieren (pillen)*, to be coated (pills).  
*Drei mal täglich*, thrice daily.  
*Durch die Nase einzuziehen*, to be sniffed up the nostrils.  
*Ebenfalls*, also.  
*Eigelb*, yolk of an egg.  
*Eingeben*, administer.  
*Einspritzung*, injection.  
*Einspritzung in die Adern*, intravenous injection.  
*Einspritzung in die Muskeln*, intramuscular injection.  
*Einspritzung unter die Haut*, subcutaneous injection.  
*Einzuspritzen*, to be injected.  
*Einzutropfen*, to be instilled.  
*Eiweiss*, white of an egg.  
*Erbrechen*, vomiting.  
*Erwärmen*, to be warmed.  
*Esstöffel*, tablespoon.  
*Etikette mit Rezept*, label with formula.  
*Flasche*, bottle.  
*Frottieren*, friction.  
*Für innerlichen Gebrauch*, for internal use.  
*Gelegentlich*, occasionally.  
*Genau*, accurately.  
*Genügend*, sufficiently.  
*Gestern*, yesterday.  
*Gift*, poison.  
*Glaskapsel oder Phiole*, glass capsule or ampoule.  
*Glasstab*, glass rod.  
*Gleiche Teile*, equal parts.  
*Gurgelwasser*, gargle.  
*Gut*, well.  
*Herz*, heart.  
*Hüfte*, hip.  
*Husten*, cough.  
*In das Auge zu bringen*, to be placed in the eye.  
*In der angegebenen Weise*, in the manner directed.  
*In der gewohnten Weise*, in the usual manner.  
*In gleiche Teile zu teilen*, to be divided into equal parts.  
*Inhalations-Apparat*, inhaler.  
*Jeden Abend*, every evening.  
*Jeden Morgen*, every morning.  
*Jeden zweiten Tag*, every other day.  
*Klystier*, enema.  
*Kochend*, boiling.  
*Kurz vor dem Schlafengehen*, just before retiring to rest.  
*Leder*, leather.  
*Löffel*, spoon.  
*Mazerieren*, macerate.  
*Messerspitze vollen*, as much as lies on the point of a knife.  
*Morgen früh*, to-morrow morning.  
*Mundwasser*, mouth-wash.  
*Mutterzapfen*, pessary.  
*Nach Anweisung*, as directed.  
*Nach Bedarf*, when required.  
*Nach dem Essen*, after meals.  
*Nachdem man die Flasche umgeschüttelt hat*, the bottle having been first shaken.  
*Nach einer Stunde*, at the expiration of an hour.  
*Nach Gewicht*, by weight.  
*Nahe*, near.  
*Niederliegen*, lying down.  
*Nur auf ärztliche Anweisung abzugeben*, to be given only on the medical man's direction.  
*Nur für äusserlichen Gebrauch*, for external use only.  
*Nur für örtlichen Gebrauch*, for local use only.  
*Ohne*, without.  
*Pinself*, to be painted.  
*Recht*, right.  
*Reiben*, rub.  
*Reizbar*, irritable.  
*Schmerz*, pain.  
*Sofort*, immediately.  
*So lange der Schmerz anhält* while the pain lasts.  
*Spritze*, syringe.  
*Stets kühl zu halten*, to be kept cool.  
*Streichen*, spread.  
*Stuhlzäpfchen*, suppository.  
*Stunde (Eine)* one hour.  
*Täfelchen*, tablet.  
*Täglich*, daily.  
*Topf*, pot.  
*Trunk*, draught.  
*Ueber*, above.  
*Uebersilbern (Pille)*, to be silvered (pill).  
*Umschütteln*, to shake (the bottle).  
*Verbandwatte*, absorbent wool.  
*Verordnen*, prescribe.  
*Von Tag zu Tag*, from day to day.

**German Glossary—continued.**

*Vor dem Gebrauch gut umzuschütteln*, to be well shaken before use.  
*Vorsicht*, with care.  
*Vorsichtig*, cautiously.  
*Während des Aufbrausens*, during effervescence.  
*Wenn der Husten belästigt*, when the cough is troublesome.  
*Woche (Eine)* one week.  
*Zahnfleisch*, the gums.

*Zahnreinigungsmittel*, dentifrice.  
*Zerreiben oder zerbrechen*, to be crushed or broken.  
*Zerstäubungs-Apparat*, spray or atomiser.  
*Zitronensaft*, lemon juice.  
*Zubereitet*, prepared.  
*Zu gleichen Teilen*, of each equal parts.  
*Zu nehmen*, to take.  
*Zwischen*, between

**ITALIAN GLOSSARY.**

*A caldo* warmed.  
*A essere aspirato dalle narici*, to be sniffed up the nostrils.  
*A frantumarsi o spezzarsi*, to be crushed or broken.  
*Aggiungere un cucchiaino ad un mezzo litro di acqua bollente, e fare inalazioni colla evaporazione*, one teaspoonful to a "pint" of boiling water and the steam inhaled.  
*Agitare la bottiglia avanti l'uso*, the bottle having been first shaken.  
*A gradi*, by degrees.  
*Al di sopra*, above.  
*A meno che*, unless.  
*A peso*, by weight.  
*Apparecchio respiratorio*, respirator.  
*Applicare con un pennello*, to be brushed.  
*Applicare la flaccia sulla ferita frequentemente, e appena asciutta ripetere di nuovo l'applicazione*, Apply lint to the wound frequently, as soon as dry repeat the application again.  
*Bacchetta di vetro*, glass rod.  
*Bollire*, boiling.  
*Bottiglia*, bottle.  
*Candela*, bougie.  
*Capsule o ampolle di vetro*, glass capsules or ampoules.  
*Ciglia*, eye-lashes.  
*Clistere*, Enema.  
*Collirio*, eye-wash.  
*Come fu detto*, as directed.  
*Come fu detto avanti*, as previously directed.  
*Cucchiaino da caffè*, dessertspoon (very few people take "tea" in Italy.)  
*Cucchiaino*, spoonful.  
*Cucchiaino da tavola*, tablespoonful  
*Cuoio*, leather.  
*Da applicarsi dietro l'orecchio destro*, apply behind the right ear.  
*Da applicarsi eggermente prima di coricarsi*, to be applied lightly at bedtime.  
*Da applicarsi sulla eruzione cutanea*, to be applied to the eczematous rash.  
*Da argentarsi (pillole)*, to be silvered (pills).

*Da bere*, drink.  
*Da instillarsi*, to be instilled.  
*Da ricoprirsi (pillole)*, to be coated (pills).  
*Da sciogliersi*, dissolve.  
*Da somministrarsi*, to be administered.  
*Da strofinarsi con un panno su cuoio cappelluto sera e mattina*, to be rubbed into the bare patches on the scalp night and morning.  
*Da usarsi localmente*, for local use only.  
*Da vicino*, near to.  
*Di giorno in giorno*, from to day day.  
*Diviso in parti uguali*, of each equal parts.  
*Dolore*, pain.  
*Domani sera*, to-morrow night.  
*Domattina*, to-morrow morning.  
*Domattina presto*, early to-morrow.  
*Dopo i pasti*, after meals.  
*Dopo un'ora*, at the expiration of an hour.  
*Esattamente*, accurately.  
*Etichetta*, label.  
*Etichetta con formula*, label with formula.  
*Falaccia*, lint.  
*Filtrare*, strain.  
*Fino a*, up to.  
*Fino a che dura il dolore*, while the pain last.  
*Fra mezzo*, between.  
*Frizioni*, friction.  
*Gargarizzare*, gargle.  
*Giacere*, lying down.  
*Giornalmente*, daily.  
*Giusto*, right.  
*Gocce*, drops (of liquid).  
*Idrofilo*, absorbent.  
*Ieri*, yesterday.  
*Il cuore*, the heart.  
*Inalazioni-inalatore*, inhalation-inhaler.  
*Iniezione sottocutanea*, subcutaneous injection.  
*Insieme*, together.  
*L'anca*, the hip.  
*La mano*, the hand.  
*La tosse*, the cough.  
*Latte*, milk.  
*Le gengive*, the gums.



**Italian Glossary—continued**

*Lo stesso*, the same.  
*Non più di 4 volte al giorno*, not more than four times a day.  
*Ogni due ore, Un'ora sì e l'altra no*, every other hour.  
*Ogni quarto d'ora*, every quarter of an hour.  
*Ogni sera*, every night.  
*Ogni due ore*, every two hours.  
*Ogni tre giorni*, every third day.  
*Palpebre*, eye-lids.  
*Pastiglie*, lozenges.  
*Pennellare la gola ogni giorno, una mezz'ora dopo colazione*, paint the throat every day about half an hour after breakfast.  
*Per iniezioni* to be injected.  
*Per pennellature*, to be painted.  
*Per pennellature alle narici due volte al giorno*, apply to the nostrils with a camel's hair brush twice a day.  
*Per sciacquare la bocca* mouth-wash.  
*Prima di coricarsi*, just before retiring to rest.  
*Pure*, also.  
*Quando la tosse arreca disturbo*, when the cough is troublesome.  
*Sera*, night.  
*Se sarà necessario* if necessary.  
*Settimanalmente*, weekly.

*Senza*, without.  
*Siringa*, syringe.  
*Sorso*, draught.  
*Spruzzatore*, spray.  
*Stoppaccio*, tampon.  
*Strofinare*, rub.  
*Sugo di limone*, lemon juice.  
*Tazza*, cup.  
*Tre volte al giorno*, three times a day.  
*Tutte le mattine*, every morning.  
*Una goccia dentro la pupilla degli occhi una volta al giorno*, a drop into the lower lid of each eye once a day.  
*Una manciata*, handful.  
*Una settimana* a week.  
*Una volta*, once.  
*Un bicchiere da vino*, wine-glass.  
*Un bianco d'uovo*, white of an egg.  
*Un giorno sì ed un giorno no*, every other day.  
*Un torlo d'uovo*, yolk of an egg.  
*Un uovo*, an egg.  
*Vaporizzatore*, atomiser.  
*Vaso*, pot.  
*Veleno*, poison.  
*Vena*, vein.  
*Versare*, pour off.  
*Vescica*, blister.  
*Vicino*, near.  
*Visiera*, eye-shade.

**PORTUGUESE GLOSSARY.**

*A*, the (feminine).  
*Acima*, above.  
*Algália*, bougie.  
*Almoço*, breakfast.  
*Alternadamente*, alternately.  
*Amanhã á noite*, to-morrow night.  
*Amanhã pela manhã*, to-morrow morning.  
*A menos que*, unless.  
*A parte dorida*, the painful part.  
*A pelle de craneo, couro (cabelludo)*, scalp.  
*A peso*, by weight.  
*Applica-se suavemente na séde da dór*, to be applied gently to the painful part.  
*Aquecido*, warmed.  
*A serem cobertas (pilulas)*, to be coated (pills).  
*A serem prateadas (pilulas)*, to be silvered (pills).  
*A ser instillado*, to be instilled.  
*A ser pincelado*, to be brushed.  
*A ser pintado*, to be painted.  
*As gengivas*, the gums.  
*Atraz*, behind.  
*Banho para o olho*, eye-wash.  
*Beber*, to drink.  
*Bem*, well.  
*Cabelludo*, hairy.  
*Calvo* bald.

*Capsulas ou ampoulas de vidro*, glass capsules or ampoules.  
*Cautelosamente*, cautiously.  
*Chiavena, Chicara*, cup.  
*Clyster*, enema.  
*Coár*, to strain.  
*Colhér cheia*, spoonful.  
*Colhér de chá cheia*, teaspoonful.  
*Colhér de doce cheia*, dessertspoonful.  
*Colhér de sopa cheia*, tablespoonful (soup-spoon).  
*Com cuidado*, cautiously, with care.  
*Como indicado nas instruções*, as directed.  
*Com precisão*, accurately.  
*Coração, o*, the heart.  
*Couro*, leather.  
*Cuidadosamente*, carefully.  
*De deitarse, á hora*, at bedtime.  
*De dia a dia*, from day to day.  
*Depois*, after.  
*De tres em 3 dias*, every third day.  
*De vez em quando*, occasionally.  
*Direito, lado*, right side.  
*Dór*, pain.  
*Em partes equaes, de cada*, of each equal parts.  
*Emquanto durar a dór*, while pain lasts.  
*Entre*, between.  
*Erupção*, the rash.

**Portuguese Glossary—continued**

*Esfregar*, to rub.  
*Estender*, to stretch, extend.  
*Esterilisar*, sterilise.  
*Etiqueta com formulario*, label with formula.  
*Exactamente antes de retirarse para descansar*, just before retiring.  
*Fios de linho*, or *lichino*, lint.  
*Flatulencia*, flatulence.  
*Friccionar*, rub.  
*Fricção*, friction.  
*Fomentação*, fomentation.  
*Garganta*, the throat.  
*Gargarejo*, gargle.  
*Garrafa*, or *Frasco*, bottle.  
*Garrafa bem agitada*, the bottle well shaken.  
*Gemma d'um ovo*, yolk of egg.  
*Gotas*, drops.  
*Hontem*, yesterday.  
*Hostia*, Cachet or wafer.  
*Inhalação - inhalador*, inhalation-inhaler.  
*Injecção*, injection.  
*Injecção intramuscular*, intramuscular injection.  
*Injecção intravenosa*, intravenous injection.  
*Injecção subcutanea (or epidermica)*, subcutaneous injection.  
*Irritavel*, irritable.  
*Lavagem de boca*, mouth-wash.  
*Lavagem para os olhos*, eye-wash.  
*Leite*, milk.  
*Mais*, more.  
*Mão cheia*, handful.  
*Mão*, hand.  
*Mesmo*, same.  
*Não*, not.  
*Noite*, night.  
*No meio de*, in the middle of.  
*O*, the (masculine).  
*Orelha*, ear.  
*Pala para o olho*, eye-shade.  
*Palpebras*, eye-lids.  
*Panella*, pot.

*Para aspirar pela ventas*, to be sned up the nostrils.  
*Para ser*, to be.  
*Para ser injectado*, to be injected.  
*Para ser triturado o quebrado*, to be crushed or broken.  
*Para uso externo*, for external use.  
*Pastilha*, tablet.  
*Pela manhã*, in the morning.  
*Pellica*, kid leather.  
*Perto (de), junto (a)*, near (to).  
*Pestanas*, eye-lashes.  
*Pó*, powder.  
*Pulverizador*, spray and atomiser.  
*Quadril*, hip.  
*Refeições*, meals.  
*Respiração*, breathing.  
*Respirador*, respirator.  
*Semana, uma*, a week  
*Seringa*, syringe.  
*Sitio*, place.  
*Sem*, without.  
*Sim*, yes.  
*Sumo de Limão*, lemon juice.  
*Taça*, large cup (goblet, bowl).  
*Tambem*, also.  
*Tampão*, tampon.  
*Todos os dias*, daily.  
*Tosse*, cough.  
*Uma gota na palpebra interior, de cada olho, uma vez por dia*, a drop into the lower lid of each eye once daily.  
*Uma hora sim, uma não*, every other hour (one hour yes, one no).  
*Uma vez*, once.  
*Um dia sim outre não*, every other day.  
*Vareta de vidro*, glass rod.  
*Vasar*, to pour off.  
*Veia*, vein.  
*Veneno*, poison.  
*Ventá*, nostril.  
*Vesicatorio*, blister.  
*Vez, cada*, each time.

**SPANISH GLOSSARY.**

*Acepillarse*, to be brushed.  
*Agua para lavar la boca*, mouth-wash.  
*Agua para lavar los ojos*, eye-wash.  
*A la hora de acostarse*, at bed-time.  
*Almuerzo*, breakfast (lunch).  
*Alternativamente*, alternately.  
*Ampollas de vidrio*, glass ampoules.  
*A no ser que*, unless.  
*Aparato, de inspirar*, inhaler.  
*Apliquese suavemente al sitio del dolor*, apply gently to the painful parts.  
*Aspiración*, breathing.  
*Atrás*, behind.  
*Beber*, to drink.  
*Bien*, well  
*Cabello (el) del cráneo*, the hair of the scalp.  
*Cabritilla*, kid leather.  
*Cadera*, hip.  
*Calentado*, warmed.  
*Calvo*, bald.  
*Candelilla*, bougie.  
*Cápsulas de vidrio*, glass capsules.  
*Cerca*, near; near to.  
*Colar*, to strain.  
*Comidas*, meals.  
*Con cuidado*, with care.  
*Con precisión*, accurately.  
*Corazón, el*, the heart.  
*Cubrirse*, to be coated (pills).



**Spanish Glossary**—*continued.*

*Cucharada*, spoonful.  
*Cucharada de postre*, dessertspoonful.  
*Cucharada de sopa*, soup- or table-spoonful.  
*Cucharadita de té*, teaspoonful.  
*Cuero*, leather.  
*Cuidadosamente*, carefully, accurately cautiously.  
*De día en día*, from day to day.  
*Derecha*, right (hand).  
*Después*, after.  
*De tres en tres días*, every third day.  
*De vez en cuando*, occasionally.  
*Dolor*, pain.  
*El*, the (masculine).  
*En medio de*, in the middle of.  
*Encías*, the gums.  
*Encima*, above.  
*Entre*, between.  
*Esterilizar*, sterilise.  
*Exactamente antes de retirarse para dormir*, just before retiring.  
*Extender*, to spread.  
*Frotar*, rub.  
*Garganta*, the throat.  
*Giro*, draft.  
*Gotas*, drops.  
*Hilas de lino*, lint.  
*Inyección entrecenoso*, intravenous injection.  
*Inyección intramuscular*, intramuscular injection.  
*Inyección subcutaneo*, subcutaneous injection.  
*Jeringa*, syringe.  
*Jugo de limón*, lemon juice.  
*La*, the (feminine).  
*La parte que duele*, the painful part.  
*Leche*, milk.  
*Llegado*, arrived.  
*Loción*, eye-wash.  
*Mano*, hand.  
*Mañana, por la mañana*, to-morrow morning.  
*Mano llena*, handful.  
*Mañana por la noche*, to-morrow night.  
*Más*, more.  
*Mientras dura el dolor*, while the pain lasts.  
*Mismo* same.  
*Nariz*, nostril.  
*No*, not.  
*Noche*, night.

*Oblea*, wafer.  
*Orden (or Pcdido)*, order.  
*Oreja*, ear.  
*Para inspirar por las narices*, to be sniffed up the nostrils.  
*Para instilar*, to be instilled.  
*Para inyectar*, to be injected.  
*Para ser*, to be.  
*Para uso externo*, for external use.  
*Párpados*, eye-lids.  
*Partes iguales de los dos*, of each equal parts.  
*Pestañas*, eye-lashes.  
*Píldoras (Mézclese y háganse 100 Píldoras)*. (*Háganse* is frequently contraeted to "H"), Pills (mix and prepare 100 pills).  
*Pintarse*, to be painted.  
*Platearse*, to be silvered (pills).  
*Polvo*, powder.  
*Por la mañana*, in the morning.  
*Potcillo*, pot.  
*Por peso*, by weight.  
*Restregar*, to rub.  
*Rociador y Pulverizador*, spray and atomiser.  
*Romperse*, to be crushed or broken.  
*Rótulo con fórmula*, label with formula.  
*Sanguijuela*, leech.  
*Según se dirige*, as directed.  
*Semana*, a week.  
*Sin*, without.  
*Sitio (or lugar)*, place.  
*Tambien*, also.  
*Tapón*, tampon.  
*Taza*, cup (drinking) or tea cup.  
*Todos los días*, daily.  
*Tos*, cough.  
*Una hora si y la otra no*, every other hour.  
*Una gota en el párpado inferior de cada ojo, una vez al día*, a drop into the lower lid of each eye once daily.  
*Una vez*, once.  
*Un día si y el otro no*, every other day.  
*Vaciar*, to pour off.  
*Varilla de vidrio*, glass rod.  
*Vejigatorio*, blister.  
*Vena*, vein.  
*Veneno*, poison.  
*Vez una*, once (one time).  
*Visera*, eye-shade.  
*Yema de huevo*, yolk of egg.

The title of 'Doctor' also of 'Quaek,' in many languages.—Lii./10,188.



# MEMORANDA.

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*The Authors would welcome any suggestions from Medical Men, Pharmacists, or Analysts.*

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